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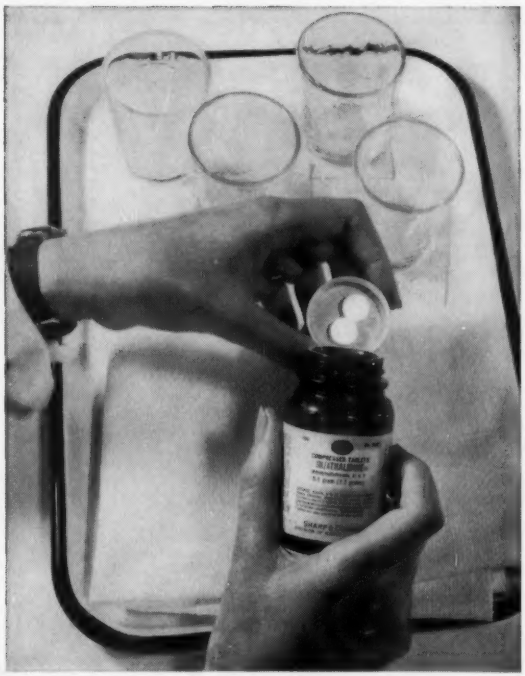

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THE American Journal OF Gastroenterology

(FORMERLY THE REVIEW OF GASTROENTEROLOGY)

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SAMUEL WEISS, *Editor-in-Chief*

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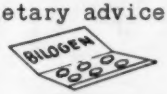
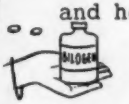
I hied myself to Dr. Jones  who reached into his experience for some sound dietary advice and into his drawer for some Bilogen samples he had  "Take two of these now with water for relief  and here's a prescription for some to keep on hand  in case you have this trouble again. But don't overload your digestive tract  as you have been, and stay away from so many rich foods. Moderation  in diet is what you need."

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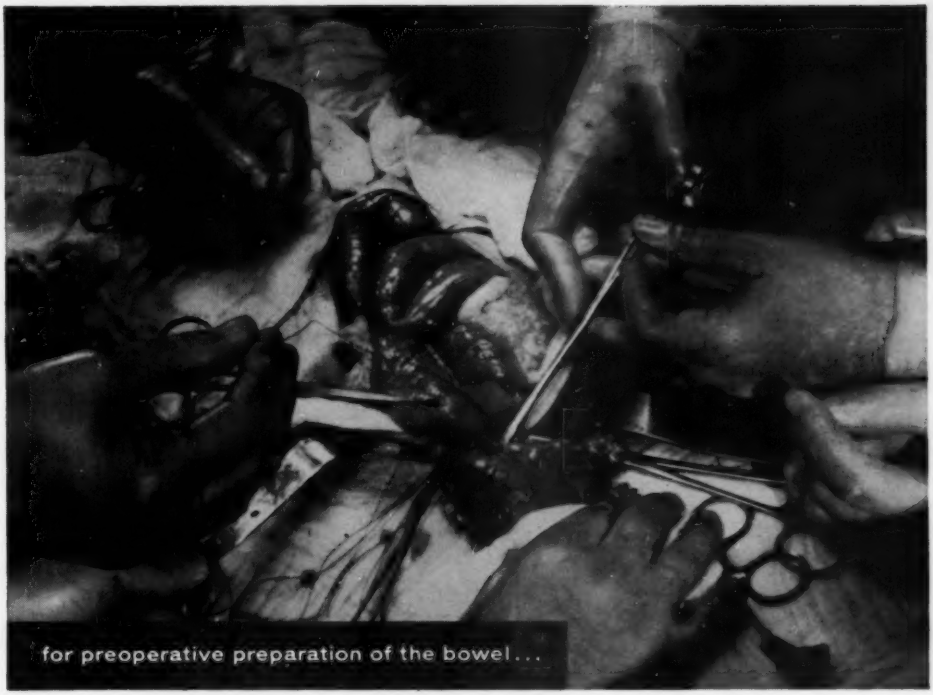

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THE American Journal OF Gastroenterology

A monthly journal of Gastroenterology, Proctology and Allied Subjects
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VOLUME 27 MAY, 1957 NUMBER 5

PANEL DISCUSSION ON DISEASES OF THE COLON*

PERRIN H. LONG, M.D., Moderator†

IRVING F. ENQUIST, M.D., M.S.‡

SIDNEY M. FIERST, M.D., M.S., F.A.C.P., F.A.C.G.§

HARRY Z. MELLINS, M.D.¶

and

PATRICK J. FITZGERALD, M.D.**

Brooklyn, N. Y.

Dr. Perrin H. Long:—I should like to introduce on the far left, Dr. Irving F. Enquist, Associate Professor of Surgery; next, Dr. Sidney M. Fierst, Clinical Associate Professor of Medicine, State University of New York, College of Medicine, State University of New York, College of Medicine at New York City; Physician-in-Charge, Gastroenterology, Maimonides and Kings County Hospital (University Division), and Attending Gastroenterologist, Brooklyn Veterans Hospital.

Next is Dr. Harry C. Mellins, Chairman of the Department of Radiology, State University of New York, College of Medicine at New York City, and Director of Radiology, Kings County Hospital Center.

Next is Dr. Patrick J. Fitzgerald, Chairman of the Department of Pathology, State University of New York, College of Medicine at New York City, and Director of Pathology, Kings County Hospital Center.

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*Presented before the Third Annual Convention of the American College of Gastroenterology, New York, N. Y., 15, 16, 17 October 1956.

†Chairman, Department of Medicine, State University of New York, College of Medicine at New York City.

‡Associate Professor of Surgery, State University of New York, College of Medicine at New York City.

§Clinical Associate Professor of Medicine, State University of New York, College of Medicine at New York City.

¶Chairman, Department of Radiology, State University of New York, College of Medicine at New York City.

**Chairman, Department of Pathology, State University of New York, College of Medicine at New York City.

Our panel this afternoon is, due to the wishes of my colleagues—who refused to prepare papers—going to be very informal, and I would think that if any in the audience feel the urge to ask a question of any kind, and will try to catch the eye of the moderator, I will interrupt the individual at the end of whatever he is saying and see that the question is answered.

There was no reason whatsoever to select me as moderator of this panel. I am a very healthy individual. I eat and drink anything. Outside of the slight irritation of the stomach that comes on upon occasion, with which many of you may be familiar, I have never had a stomach upset and, as I grow older and wiser, I have had fewer of those. (Laughter)

So today I should like to start off this panel by throwing out a word or two about something I know nothing about, namely, constipation.

I checked the other day to get the gross value of the sales of laxatives in this country, and I find, much to my amazement, that this amounts to over a quarter of a billion dollars a year. I can reach only one conclusion from that figure, and I am going to ask Dr. Fierst and Dr. Enquist to start right off—Dr. Fierst, is it because the American people are the laziest and most temperamental people, or is there another answer as to why the gross sales of laxatives are so high?

Dr. Sidney M. Fierst:—I think a good deal of constipation may be produced by the fact that in America the mothers seem to be oversolicitous. Too much attention is paid to bowel habit and bowel training in the young, and this may be expressed in later life with a good deal of bowel consciousness.

I think, also, that the life in America may be at too rapid a pace, especially in urban environment. One gets up a little late in order to catch the morning train, grabs a little toast and orange juice, and maybe a little coffee—very little else—and rushes down to catch the 7:50 train, or the subway, and then is constantly on the go, with very little time out to carry out normal function, so that natural habit becomes suppressed, and I think this leads to constipation, also.

To a certain extent I think that doctors may be a little bit to blame in that they impress on patients that a regular bowel movement every 24 hours is essential to ordinary existence.

There is a story told about a young girl who went to a doctor complaining of a fluttery feeling and a little headache, and the doctor asked, "Well, how often do you move your bowels?"

She said, "Oh, every 24 hours."

"Well, you are constipated."

"But I move them every 24 hours."

"Well," he said, "you move them 24 hours too late." (Laughter)

I think to a certain extent we have to put some blame on ourselves for that, but I think to a great extent constipation is the result of our mode of living. You don't find too much constipation in rural areas, where natural–

Dr. Long:–Have you ever been in a rural area?

Dr. Fierst:–I have been all over–Kentucky included–up until the age of 13 I lived in Cooperstown.

Dr. Long:–I came from Bryan, Ohio, where I lived for 21 years of my life, and my father was a general practitioner. He is still alive at 95, and, fortunately, retired a year ago from practice. I imagine a doctor can't go on too long in practice. One of the things I have always known about the practice is that people in small towns of about 7,000, who were suffering from constipation, in those days probably still all went to Battle Creek, and that is where they got their constipation, on one of those diets at the Post Sanitarium.

Is it laziness and lack of habit, primarily? I like to think it is because people are lazy, to some extent or other.

Dr. Fierst:–To a good extent, yes.

Dr. Long:–Does anyone on the panel disagree with that? Dr. Fitzgerald, what do you know about constipation?

Dr. Patrick J. Fitzgerald:–Relatively nothing.

Dr. Long:–Dr. Enquist, do you have any comments on it?

Dr. Irving F. Enquist:–No, I don't.

Dr. Long:–Is it a surgical problem, as you see it in ward surgery?

Dr. Enquist:–I have heard the statement made that there isn't a surgeon with any experience to talk about, who hasn't done a transverse colostomy for a fecal impaction. About the only time I encounter constipation as a real problem is in rare instances of fecal impaction, with complete colonic occlusion.

Dr. Long:–Dr. Fierst, have you ever seen such cases?

Dr. Fierst:–I was planning to ask Dr. Enquist about that particularly, and the problem which I think in that case is primarily a surgical one.

Dr. Long:–How about Hirschsprung's disease?

Dr. Fierst:–Well, Hirschsprung's disease is a different disease from constipation which is perhaps a result of poor training habits in children. There is an organic basis for true Hirschsprung's disease. Demyelinized nerve segments and absence of the intramural ganglia of Auerbach's and Meissner's plexi are the pathologic criteria. One can easily make the diagnosis by the history. According

to Swenson, the history in a true Hirschsprung's disease originates at birth, but the children come in with poor bowel habits. The symptoms have not become identified by the mother, and the problem does not become manifest until the child is at least two or three years of age.

Dr. Long:—Dr. Mellins, would you be able to diagnose constipation from a roentgenogram?

Dr. Harry Z. Mellins:—If you are discussing the first type of constipation, I would say we cannot be of any help. I think the old practice of diagnosing various types of spasm in the colon in barium enema studies was more misleading than helpful.

With regard to Hirschsprung's disease, I would say that the diagnosis should be quite accurately made by x-ray examination provided the fluoroscopist is aware of the importance of the oblique position. He will distinguish between the localized aganglionic type of megacolon, in which there is a localized area of dyskinesia in the distal part of the colon with dilatation above it, and the idiopathic type of megacolon, which is usually of anal origin, be this due to anal fissures, or anal clefts, or anal ulcers, or anal personality.

Dr. Long:—Dr. Enquist, you had your finger up.

Dr. Enquist:—A thought came to my mind as Dr. Mellins talked about areas of spasm in the colon. I have recently run into an expression and I don't know really whether it has any anatomical significance or not, and that is "Cannon's ring", the theoretic junction between the primordial midgut and the hind gut. At one time I was interested in the effect of morphine on the gut in postoperative cases, and we and our radiologists thought we saw a higher incidence of spasm at the so-called area of Cannon's ring, than elsewhere in the colon. Is this true, Dr. Mellins?

Dr. Mellins:—This (Cannon's ring) is one of the areas in which it occurs. The older anatomists differentiated about six areas in the colon, from the cecum to the sigmoid, where there were larger circular areas of musculature. In these areas the segmenting action of the colon probably occurs, and if you happen to catch one of these areas in contraction, you get what is apparently an area of narrowing. This is physiological.

Dr. Long:—I never heard of Cannon's ring before.

Dr. Fierst, suppose you had a "baby" from Brooklyn come in, age from 50 up, with a complaint of constipation, what would you do? How do you treat constipation?

Dr. Fierst:—One must recognize that constipation is only a symptom. I think that one should take a complete history of such a patient, including personal habits; the duration of the constipation, whether or not it is of recent onset and

what the previous bowel habit was. Then one must delve into the dietary habits. Finally a complete and thorough physical examination is necessary. One thing I think one should stress is that a part of any physical examination is a sigmoidoscopy. One should examine both the external aspects of the anus as well as the full length of 25 cm. in order to determine the tone of the internal sphincter muscle, whether there are any fissures or anal ulcers present, and also look for pathology higher up.

Probably 50 per cent of colonic lesions can be visualized if care is taken. I have seen patients who have been sigmoidoscoped but the sigmoidoscopist neglected to explore the hollow of the sacrum, which is a common site for carcinoma, and if one is not careful, one can go right past this area.

Then, following the sigmoidoscopy, I think one should take some of the stool and see if it is guaiac positive. This can be done as routine on every patient to determine whether there are any bleeding areas in the bowel. The patient is then subjected to a barium enema, after proper preparation. I think that proper preparation of the bowel should mean that the bowel is thoroughly cleansed.

I personally prefer castor oil to licorice powder as a preparation. I think castor oil leaves the bowel quite dry, so that good mucosal detail is obtained.

Later on I hope you will ask Dr. Mellins about various technics for barium enema examination. Personally I prefer adding a little tannic acid to our barium preparation, which gives a good evacuation film, and I think that air contrast enema should be part of all barium x-ray examinations. After ruling out local or colonic organic disease as a cause of constipation, one has to determine from the personality of the individual whether there is an apparent personality defect or whether it is a matter of deficient gastrocolic reflex.

We see a lot of women, elderly women–well, not elderly–I am getting towards 50 myself–women in their late 40's and early 50's, who are on reducing diets and, as a result take in very little food. Now, one of the causes of constipation is a lack of this gastrocolic reflex, and I think by correcting the diet habits of the individual, one can correct a good proportion of constipation.

Another cause of constipation, I think, is the fact that the individual does not take time to have a normal bowel movement and that, too, can be regulated.

In some patients I use an hydrogogue, something like the psyllium seed derivatives, or plantago preparations, with a good deal of satisfaction. I think these preparations absorb water as much as twenty-fold, producing a bulk, which is an increased stimulus to excretion. They also, to a certain extent, have a demulcent character.

There is one other problem which I, as a gastroenterologist, encounter, which annoys me a bit, and that is, in the patient being treated for ulcer, with

an alumina gel preparation. The detail men come in and hold forth in a very profound manner that their particular alumina gel preparation is superior to other preparations, adsorbs acid and does not form constipating aluminum chloride. The proof of the pudding is that many of these preparations are coming onto the market with added magnesium hydroxide, or magnesium salts. Alumina gel is constipating, and I feel that we, as physicians, should not surrender our birthright in using amounts of magnesium hydroxide, or aluminum hydroxide as prescribed by the drug companies, but recognize that each individual requires varying amounts of these preparations.

Dr. Long:—I was in error. I should have said from 35 years up. I was figuring from 50 up you go to see the doctor about constipation. (It has already cost them $75)

Dr. Fierst:—We don't get those. One must recognize that systemic conditions can produce constipation. Pernicious anemia and lead poisoning may both manifest themselves with constipation. Carcinoma of the cecum or right colon must be differentiated. Certain less common diseases like hypothydroidism and hyperparathyroidism may also present with constipation. By careful history, physical and x-ray one can differentiate purely local colonic disease from the systemic causes of constipation. Therefore, the investment in time and money is worthwhile.

Dr. Long:—I have been asked to say something about cleansing the colon. I heard you say something about that in passing, Dr. Mellins, in one of our conferences the other day. What do you want for a barium enema?

Dr. Mellins:—I am not prepared to take sides in the matter of whether it be an ounce and a half of castor oil, or two drams of compound licorice powder. It seems to me these are the two best media to use, and I think the patients have a little more psychological resistance to castor oil, by name, than they do to licorice powder. I have gotten good results with both.

I would have a word, however, to say about enemas which I think are poorly done most of the time, and need not be.

A saline solution, which the patient can easily make by using a quarter of a teaspoonful of salt to a quart of water, is the best solution to use. If one uses plain tap water, one may run into water intoxication in patients with dilated colons, especially in children. Irritants like soapsuds are not usually of any value.

A good many of the ambulatory patients will sit down on the water closet and take their enema sitting on the toilet. This, of course, does nothing but wash out the rectum and is an absolutely useless procedure for barium enema preparation. If you ask the patients how many are doing it and how many are otherwise instructed, you will be amazed.

To go to the hospitalized patients, you will find every nurse since time immemorial has been taught to give an enema with the patient lying on the left side, as this is supposed to be less painful to the patient. What happens when the patient lies on the left side is that all the gas is pushed up to the right half of the colon, and all the fecal matter floats up to the right side of the colon. The patient evacuates clear returns even though the colon contains almost as much feces and gas as it did at the outset.

In order to do a proper cleansing enema, one quart usually suffices, provided only one-third is given with the patient on the left side. After the rectum and sigmoid are filled and initial spasm is counteracted by a little patience and waiting, the patient should be turned on the right side and the remainder of the enema given. In this manner the gas and fecal matter are not pushed into the right half or descending portion of the colon. One, or, at the most, two enemas of this kind are sufficient for good cleansing, and they should be given two hours before the barium enema study.

I think that this is all I have to say about the preparation, but I would like to say one or two other things, if I may.

Dr. Long:—Yes, certainly.

Dr. Mellins:—First, I think that any examination in which the barium mixture is not penetrated so that you cannot see one loop through the other loop, is inadequate.

The comment Dr. Fierst made about the use of tannic acid, I would agree with. It is an error, I think, to omit a lateral view of the rectum and rectosigmoid, because one of the two most difficult areas to examine clinically is the area directly proximal to the tip of the examining finger, or the area that the sigmoidoscopist may pass by in the hollow of the cecum.

Finally, I would say that there are only three ways that I know of to be certain that you have filled the colon. One is to identify the terminal ileum; the second is to identify the appendix, and the third is to identify the ileocecal valve. I feel that the latter is by far the best, for many reasons: first, if you train yourself to notice the ileocecal valve, you will pick up lesions of the valve you might otherwise miss, and second, you will, in filling the colon, more often be able to let a measured amount of barium into the terminal ileum, so that the sigmoid is less often obscured on the film.

Dr. Long:—I am intrigued by what you have said about one thing. It reminds me of the poor ambulatory patient who has to give himself an enema. You can see how easy it is in most modern bathrooms in the houses of today to take an enema. I had a barium enema once in my life. There I was with my enema bag. I could not hold it in my hand, and I had no place to hang it, so I had to screw a coathanger to the back of the door and deface the door.

Then I had to try to curve myself around between the legs of the wash stand, the base of the toilet, and the radiator, to get on the floor. This was difficult and the enema results were poor.

Then I thought about using the tub, and I was afraid I would fall in the tub, and I tried to hook my toes to the shower ring above me. It did not work. Just try to give yourself an enema.

I have brought this up because it came to mind. Now I think we have gone far enough on this particular subject and have wandered a bit, which I think is a good thing, but now I should like to ask Dr. Enquist the next question. I will start off with him.

What do you think should be the treatment for the first attack of diverticulitis, Dr. Enquist?

Dr. Enquist:—There is no question that most first attacks of diverticulitis are being handled by internists and general practitioners, who are seeing the patients in their offices, occasionally in the hospital, and probably quite often at home. The patient is usually tided over that episode very effectively.

If, however, I were posed with a patient with a severe bout of diverticulitis, and I was convinced this was the first attack, and the patient had severe abdominal symptoms and signs, namely, tenderness, leucocytosis and fever of 102° or 103°, I think on the basis of what has been showing up in the surgical literature recently that I would recommend to that patient to have the involved area resected if the local conditions warranted.

I should like to cite one case which obviously alone does not make the point. This was a 65-year old dentist whom I saw about three months ago. He came in with an acute abdomen, and the resident called me. We saw this man with a very hot abdomen and fever, with free air in the peritoneal cavity. We explored him with the thought in mind that he probably had a perforated diverticulitis, and that we probably would do a transverse colostomy. We found, however, that this man had a very good-looking colon, with multiple diverticula. We found the involved area, and proceeded to resect it. Six days later he left the hospital feeling perfectly well, and we have since had barium enemas on him, and he shows no evidence as yet of diverticula in his remaining colon.

Dr. Long:—Dr. Fierst, what do you think about this?

Dr. Fierst:—I am mostly conservative in the management of the cases of diverticulitis, particularly in a patient who comes in with an acute, red-hot abdomen, who has not perforated. I am a little afraid of operating or resecting a patient with an acute diverticulitis. I would much prefer, as in acute cholecystitis, using the same analogy that Dr. Enquist presented, to wait and see if the inflammation subsides.

If a localized abscess forms, of course, one has to drain it. I think an exclusion procedure, with later resection, might carry a lower long-term mortality. I think if it is a mild case of diverticulitis these patients can be handled medically, with diet and antibiotics. I prefer the use of sulfonamides in this particular type of case.

Dr. Long:—Why do you prefer sulfonamides?

Dr. Fierst:—Particularly the insoluble sulfonamides, sulfathaladine, or sulfaguanidine, or sulfasuxidine. These can be given over a longer period of time. They do seem to cause a softening of the stool. There is less constipation, and the results seem to warrant their use. There is less resistance, particularly in the development of a staphylococcal enteritis, which will occur with the long-term use of the broad spectrum antibiotics.

Dr. Long:—In acute cases do you use soluble sulfonamide, or insoluble sulfonamide, or antibiotics, when you have your acute phase, with tenderness and rigidity, and a real bellyache, and all?

Dr. Fierst:—During that brief period I prefer the use of the broad spectrum antibiotics, and then to carry the patient along with the sulfonamides until after the acute phase is over, because I think systemic as well as local manifestations have to be treated.

Dr. Long:—Do you make the diagnosis of diverticulitis in every instance by barium enema, Dr. Mellins?

Dr. Mellins:—As soon as you say "in every instance", the answer to almost any question is no, but I would think that we can make the diagnosis in a great proportion of cases and can find evidence of superimposed inflammatory changes in a goodly number of those who have diverticulosis.

I would think that our problem was perhaps more often the distinction between diverticulitis and carcinoma, about which we will perhaps have something to say later on. The signs of diverticulitis fall into two groups: 1. signs of acute inflammation, and 2. signs of an older condition. The acute type reveals spasm and coarsening of the mucosa in an area of diverticulosis; the signs of a more long-standing infection, are pointed diverticula, or diverticula blocked at the neck, and associated mucosal changes in the region of the diverticulosis.

Dr. Long:—May I ask you this question: are there any tricks you have to be aware of in order to demonstrate the diverticula, any special things that a radiologist knows, so that occasionally you have a patient who seems to have all the signs and symptoms of, let us say, left-sided appendicitis, and you feel quite certain that the patient has a diverticulum, or diverticula, and you get an essentially normal barium enema—are there any tricks you may hide behind, or anything like that?

Dr. Mellins:—The easiest diverticulum to miss is the solitary diverticulum with localized inflammatory changes at the neck, or one which is packed with fecal matter. If one uses a well penetrated technic, one will demonstrate diverticula except where they are blocked at the neck.

I am not aware, in an experience of 4,000 colon examinations done by myself, or my associates, over a period of three years, of any case of proved diverticulitis in which the barium enema was normal.

Dr. Long:—You used the phrase a minute ago "a well-penetrated", which, to tell the honest truth, I heard for the first time this morning when you used it, in x-ray comment. I wonder if you will explain a bit what the "well-penetrated" is. It may be of interest to some of our listeners.

Dr. Mellins:—It may be that this is a blacker film than many of you are used to but I think it is important to be able to see all limbs of the colon even though they are superimposed on one another. If one cannot see them distinctly, the film is not sufficiently penetrated. Those of you who are close up can identify all of the curls of the sigmoid and see one loop through the other.

Dr. Long:—Thank you very much. Dr. Mellins showed us this morning a beautiful film of a "well-penetrated" chest, and it was the first time I had seen that, and it was a very interesting technic.

I am sure Dr. Fitzgerald has something to say, because diverticulitis is of interest to pathologists occasionally.

Dr. Fitzgerald:—Dr. Enquist and Dr. Fierst mentioned two different aspects of a problem which a pathologist resolves a lot easier for he sees both surgical pathological material and autopsy material. The incidence of the disease in these two different areas suggests the reasons for some of the divergent views in regard to treatment of diverticulitis.

The surgeon is apt to see the acute abdomens with complications, whereas those of us who also see autopsy material tend to consider the disease as essentially a diverticulosis with occasional complications. Certain women past 50 have a high incidence of the disease and only rarely, in terms of the total number of diverticuli is there the complication of diverticulitis. I think we would be more inclined to agree with the conservative viewpoint indicated by Dr. Fierst. We do see at autopsy healed diverticulitis which apparently did not send the patient either to a physician or a hospital.

There is a significant association beginning to appear now between the presence of diverticulosis, or diverticulitis, and carcinoma. We have a greater number of people over 50 in the population and probably fewer cases with diverticulitis succumb today because of antibiotics and better treatment. Thus one would expect the two diseases to occur more frequently together.

So, one cannot dismiss diverticulosis lightly and let it go at that, because the association with carcinoma, though it is still rather low in percentage, probably is considerably much higher than the literature would indicate, and I am sure all of you have had experience with the association of the two diseases occurring in the same patient.

Dr. Long:–I am going to introduce a mystery disease. In the last two weeks two people have told me this tale. These are people between 45 and 55 years of age, and they have been bothered in the past by waking up with a definite pain in the rectum. It hurts them, and they get up and go and sit in the bathroom for a while, and it goes away. They go back to bed, and it comes back again. It is very annoying. They have been to their physicians, and in both instances the physicians are competent physicians in Manhattan, who have found nothing wrong with the patient.

Now, what about these pains in the rectum? We have heard a great deal about pains in the rectum in another sense, but what causes these? Patients wake up in the night and have the pain, and it is very sharp. It passes off and it may occur again that night, or a month or two later, or weekly. What do you think about this? Why do they have these pains?

Dr. Fierst:–Were these all male patients?

Dr. Long:–My series of two are male patients.

Dr. Fierst:–One must not lose sight of the fact that congestion of the prostate and prostatitis can become manifest with anal pain and that it will occur mostly at night. The patient gets up and micturates, and is somewhat relieved. Sometimes a full bladder may produce symptoms of anal pain.

This problem of proctodynia, or painful rectum–

Dr. Long:–Is that the name of it?

Dr. Fierst:–Yes–is a very real one. It may be associated with just spasm of the levator ani muscle, which can cause it, but I think in most of these people of 45 and 50 it may be associated with prostatic congestion and midprostatitis.

Dr. Long:–Does it occur in younger people?

Dr. Fierst:–One of my residents came to me once with a similar problem. I think it was on the same basis.

Dr. Long:–You weren't concerned about it. (Laughter)

Dr. Fierst:–I am a gastroenterologist. I am not a proctologist, but I think I might have a good explanation of these cases.

Dr. Long:–I think of another patient with a pain in his rectum which was possibly proctodynia. He called me up when he was in Baltimore, and said he

would like to come up and have a physical examination. I had to go away so I turned him over to a very good friend who listened to his story. He was rather curious as to whether there could be something in the sigmoid or rectum which could produce this patient's pain and among other things, he did a barium enema. Why he did this, he said he never knew, but he did it. This was nine years ago, and in the cecum they found a small early carcinoma which was resected. The man has been perfectly well ever since.

Without the barium enema the lesion would never have been found. It had nothing to do with pain in the rectum, and it just happened to be picked up. The patient is perfectly well, and by this device I can bring up discussion of carcinoma of the colon.

I am going to ask Dr. Fitzgerald first to bring us up to date. He spoke about the fact that because we are all living longer, carcinoma of the colon is becoming a greater hazard to the older age group. What is your point of view on this subject, Dr. Fitzgerald?

Dr. Fitzgerald:—It is quite presumptious of me to talk about carcinoma of the colon to the College but, having had a little contact with students and interns, I find that one can never oversimplify or overemphasize fundamentals, and even with our professional visiting staff certain basic facts are frequently forgotten.

Roughly 75 per cent of all carcinomas of the bowel occur in the rectum or rectosigmoid. Fifty per cent occur within reach of the examining finger, and almost 75 per cent are certainly within reach of the sigmoidoscope.

It is the opinion of most surgeons and pathologists that a significant percentage of carcinomas of the colon arise from polyps, or papillomas, or adenomas, if one wants to lump all together. Certainly one sees a very high percentage of polypoid lesions which, upon examination, will show areas of obvious carcinoma, even though there is no invasion of the stalk nor extension to the mucosa. The shorter the lesion, the flatter, and the more the circumference of the bowel it occupies the likelier it is to be associated with carcinoma, even if it does not cause the cancer. In general, the more extensive the lesion in terms of bowel wall involvement, the more one should suspect it of being a carcinoma.

I would like to emphasize a consideration of large papillary adenomas, the villous adenomas, of the rectum. Although considered a rare lesion, we have seen two in the past year. If the surgical pathologist is to properly evaluate these, and other lesions, he should have more than a mere snip of tissue in order to get an extensive sample wherein to diagnosis the benign or malignant lesion. I think it is much better to cause the patient some temporary distress and get a big piece of a little polyp rather than have us get the big human specimen a few years later because the serious lesion was missed.

Concerning rectal cancer and early diagnosis: I notice that the American College of Gastroenterology has an escuthcheon. I believe something important is missing. I think one little quadrant in it should be set aside for something from Master John of Arderne, a 14th century surgeon. You may recall a frontispiece in *Cancer* (**3**:567-570, 1950) showing a picture of him putting his finger in the rectum—and I think that one quadrant of that shield ought to carry a finger, at least, and you might dress it up with the nicety of the English 15th century translation of the Latin text:

"*Putte ye leche his fynger into ye lure* [fundament] *of ye pacient. . . .*"

Dr. Long:—Dr. Mellins, I should like to ask you a question. Have there been any surveys in people over 45 years of age, people who have no complaints, but whom you might interview in front of this Hotel and find out how many have polyps? Do we know anything about that?

Dr. Mellins:—There are surveys which are very close to that. I am not certain that I could quote the statistics too accurately, but I have some statistics of my own that are related. I was, for two years, the radiologist at the Cancer Detection Center of the University of Minnesota, where we did routine double contrast air studies on all patients who attended the clinic and met one of the following criteria:

1. Evidence of adenomas at proctoscopy or sigmoidoscopy.
2. A hemoglobin under 11 gm.
3. A family history of carcinoma of the colon.

The incidence of polyps, demonstrated radiologically, was perhaps 1.5 per cent. Another series which I personally controlled in private practice in a period in which we did 2,500 colon examinations, for all causes, in hospital and private practice, and in which a routine air contrast examination was done on every single examination, demonstrated polyps of the colon in 2.59 per cent of the patients.

If one reads the account of Dr. Welin's work, in Malmo, Sweden, in which he used some of the newer colon evacuants, principally phenylisatin, I think, as the preparation, one finds that he was able to raise the incidence of polyps of the colon, seen radiologically, to something in the neighborhood of 12 per cent. This is in agreement with autopsy statistics for the incidence of polyps of the colon, as I remember them.

Our method was not as heroic as that, and we did just one single air contrast film, which I can demonstrate to you. I should like to tell one story relating to this method and perhaps show a film.

At one of the best hospitals in the city, a small polyp of the colon was detected in a woman who was bleeding about two years before the story begins.

She was reluctant to have it resected. It was about the size of an eraser at the end of a pencil. She left to go to a large diagnostic clinic. She was examined there by routine barium examination, and was told the colon was normal. She returned home, but the films from the first hospital reached the clinic after the patient had left. One film showed what looked like a polyp of the sigmoid. A letter was sent to her stating that she had better have the examination repeated and, if the polyp were found again, an operation would be indicated. This was in opposition to her own wishes. She had been happy to have a normal report the second time around, and she did not have any further examination done.

Two years later, because of recurrence of bleeding, she came to us, and in precisely the same location as the small lesion had been found before, there was now a larger lesion, with infiltration of the wall, which both radiologically and, later, pathologically, was a carcinoma. The original lesion was minute, and there is no question in my mind that in this case and in many others, that we can follow the natural history of the development of cancers.

I should like to show one film, if I may.

(Film) This is a routine study. I am leaving out the spot films and will just show the larger film. This is a well-penetrated film made with 115 kv. Only the people in the first row can see this, but there is, where the arrow points, a filling defect, representing a polyp shown again on the air contrast that was done the same day.

This was a routine study and this method depends upon not filling the terminal ileum too much. We make it a rule always to repeat the examination even though a polyp appears to be present on two different films the same day.

This was repeated and the polyp again found, and the patient was operated upon. It is this kind of polyp that is far more important, but less dramatic, than a large, frank carcinoma.

I wonder if Dr. Fitzgerald will have something to say about that.

(Film) Here is a polyp on a long stalk. When the air contrast was done, the polyp was blown around in the other direction, and now the stalk goes up here. It is in this kind of polyp that I think the incidence of malignancy is decidedly less than in the sessile polyp.

If we bend our efforts, we ought to demonstrate polyps of the colon in at least 2½ out of every hundred colons we do. Whether or not they are significant, and what should be done about them, is a problem which other people should perhaps decide.

Dr. Long:—Dr. Fitzgerald, I believe is a little confused. Would you ask him the question again.

Dr. Mellins:—Well, the question has to do with the incidence of malignancy in polyps, and whether the gross characteristics bear any relationship to the histologic specimens.

Dr. Fitzgerald:—I skipped over that originally, but I think Dr. Mellin's point is right. One is certainly far less worried about the polyps with a good stalk than with sessile, flat, or adenomatous lesions, and papillomata. There is a good inverse relation between the length of the polyp and the decreased tendency toward malignant association as compared to the adenomatous lesion. Papillomata have a short, wide base. They, of course, are far more likely to show malignant degeneration.

I am a little dubious about the incidence figures of polyps at autopsy, because huge autopsy figures have not been gotten together from various groups in the country, and in almost every disease we are beginning to learn something about geographical and ethnological factors that influence disease.

I think the percentage should be true for most of the hospitals on the incidence of malignant degeneration, and I think one has to qualify the type of lesion he is describing. The polyp on the long, thin stalk, again, has a relatively low incidence, at least of association with metastases. Maybe those polyps are in an unfavorable position to extend very quickly into some vessel, whereas the lesions that cover the mucosa and submucosa have a more amenable area wherein they may invade vessels.

The incidence varies in the figures from 5 to 80 per cent, depending on the pathology. In the type of polyps shown here, and much smaller ones, probably 10 to 15 per cent with associated carcinoma is more likely, but the adenomatous and villous papillomata must go close to 55 or 60 per cent. In most of the villous papillomata followed five years, there has been a high percentage of associated lymph metastases, and I think they should be followed very carefully.

Dr. Long:—I regret that I must leave the panel because I have to catch a train. I am going to turn it over to Dr. Fierst, and I hope, as I turn it over to him, that Dr. Enquist has something to say.

Dr. Enquist:—Dr. Long's question seemed loaded as I sat here, because he asked about the incidence of polyps in asymptomatic people 45 years of age and over. I worked with Dr. Mellins at the University of Minnesota, where the Cancer Detection Clinic was set up to study asymptomatic people over 45 years of age.

In eight years—and I recently had Dr. Wangensteen's permission to study these same polyp patients to find out what was occurring there—the incidence in 7,600 patients examined was 11.5 per cent. Practically all of these were in the rectum and sigmoid, as you might expect because it is the area which is available to proctosigmoidoscopy. Each patient in this center, however, is fol-

lowed again at yearly intervals, and though at the original examination only 11.5 per cent were found to have polyps, another 7.5 per cent were found in one or the other of their recheck examinations to have a polyp or polyps in the rectum or colon, giving a total incidence in these patients of 19 per cent.

Now, this is a selected group, and it must be admitted early that all the small, sessile, mucosal excresences were included. There was a high percentage of lesions less than 6 mm. in diameter, so that the high incidence can be partially attributed to this.

I want to point out also, although I think Dr. Fitzgerald did so very well, that the incidence of polyps in autopsy studies has varied between tremendous extremes. Lawrence had one of the largest series reported, and he had an incidence of 2.3 per cent, and Atwater and Bargen, at the Mayo Clinic, went over 200 consecutive autopsies and found the incidence there, after examining the entire colon with a magnifying glass, to be 69 per cent. Obviously they were including many sessile mammilations and small lesions.

In closing this discussion, I will state that we had patients in the series with one or two of these very tiny polyps, discovered by proctosigmoidoscopy, who, during their routine barium air contrast enemas were found to have one or more polyps in the remainder of the colon. Thus the finding of a small sessile mammillation can be used as a justifiable reason for performing a barium enema contrast study, because some polyps, and even an occasional cancer, were found in the colon as a result of this discovery in the rectum.

Dr. Fierst:—Dr. Enquist, is there any difference in the management of the patient with a single demonstrable polyp, and the patient who has two or more polyps?

Dr. Enquist:—Are we talking now about polyps available to the proctoscopist, those he can reach through the sigmoidoscope?

Dr. Fierst:—In other words, both. You could find two polyps within reach of the sigmoidoscope—that is one type—and the other type is the patient in whom you find a polyp on routine sigmoidoscopy, which I emphasized before should be done as part of a routine physical examination. Having found a single polyp in the rectum, a barium enema is ordered, and you find other polyps in the flexure or the transverse colon.

Dr. Enquist:—There is no question in my mind that all polyps available to the sigmoidoscopist—and I am talking about the growth described as the polyp—by all means should be removed for biopsy, if they are large enough to be significant, because the preponderant majority of these small lesions will be benign. Also, in those in whom malignant degeneration has occurred, that will nearly always occur first at the tip, and therefore many may be malignant there, but they do not show invasion of the wall. If invasion is shown, they must be

considered frank carcinomas, and an abdominoperineal or other form of operation should be carried out.

So that I think definite polyps available to the sigmoidoscopist can be treated by him through the scope. The patient who has a single lesion in the rectum and another in the splenic flexure, should have the lesion in the rectum removed and submitted for biopsy, and laparotomy should be carried out for proper treatment of the polypoid lesion. I am not prepared to state which is proper treatment for a polypoid lesion in the colon above the rectosigmoid. There are proponents of several different methods of treatment. I think most surgeons would do a simply polypectomy and carry out a frozen section examination, and if there were invasion on the frozen or paraffin section, carry out a resection. There are several well known surgeons who feel that a primary, small, segmental resection should be done for each polyp of the colon. They are in the minority when compared with those who advocate a primary polypectomy.

Let me bring in another question which I think you were leading up to: what is the treatment of the patient with two or three or more polyps in the colon above the rectum?

Personally, I feel that two definite polyps, in widely separated segments of the colon, are best treated by a subtotal colectomy, and there are arguments for and against this. There are surgeons—and I will conclude with this—who feel that even a single polyp in the colon, above the rectum, demands a subtotal colectomy because of the high incidence of multiplicity of these lesions, and also because of the high incidence of multiple carcinoma of the colon. I am not prepared to give the final answer to this question.

Dr. Fitzgerald:—There is one thing that Dr. Enquist said, that I wonder if he would qualify. Did he say that with any invasion or evidence of invasion of a polyp one should go ahead and do an abdominoperineal operation? I assume he meant invasion of the bowel wall, not of the stalk of the polyp. Pathologists make a diagnosis of carcinoma not infrequently in polyps but I doubt if we would advise abdominoperineal operations for a small focus of carcinoma out at the tip of a polyp.

Dr. Enquist:—I agree with you and stand corrected, if I made that statement. I have recently been involved in a minor discussion about the incidence of lymph node metastasis in small malignant polyps which showed no invasion through the *lamina propria,* treated by resection, in which there were involved lymph nodes at the time of removal of the segment.

I wonder if you, Dr. Fitzgerald, have seen such a malignant polyp; one in which there is no invasion through the *lamina propria,* but in which the surgical specimen happened to show lymph node metastasis?

Dr. Fitzgerald:—I think the realization has grown upon surgical pathologists that whether a lesion breaks through a membrane, or into a muscle is of

some importance, but there are many other more significant factors. The amount of the blood or lymphatic vessel involvement is, of course, most important and that is why all surgical pathological material has to be carefully examined for the extension of the lesion into vessels as well as for the extent of invasion of the wall. Elastic tissue stain for blood vessel involvement is as important as depth of muscle penetration. The significant feature is not that a lesion gets into the wall, but whether it gets to the lymphatics or blood vessels, tissue planes, cavities, or other routes of dissemination.

Dr. Fierst:—I should like to just bring up the difference between isolated adenomatous polyp and the patient who comes in with a history of polyps. Do you find any pathological difference in the cases with familiar polyposis and those found with isolated adenomatous polyp?

Dr. Fitzgerald:—Not histologically—usually more frequent, but individually nothing to distinguish them that I know of.

Dr. Fierst:—Can you differentiate them roentgenologically? Maybe the x-ray picture of multiple adenomatous polyps will be found in one, two, or three of a grouping, as opposed to polyposis.

Dr. Mellins:—Looking at an individual polyp in either case, I am not aware of any distinction that I can see. I do not remember being aware of any differential characteristics.

Dr. Fierst:—But the number of polyps is what caused you to make the diagnosis, and the history?

Dr. Mellins:—Yes. I wonder if I might add a word here about the examination for polyps in a colon in which a carcinoma has been found. I think that this is very important, and when one encounters a carcinoma of the sigmoid or any other portion of the colon, one should repeat the examination after careful preparation, to determine whether there are any other lesions above the one found. This may help the surgeon in determining the extent of his resection.

Dr. Fierst:—That is simply what I was trying to allude to. I think one should be prepared—and I will ask Dr. Enquist whether he agrees with me—for a radical operation, with a familial history, and adenoma of the colon, when more than one polyp is found on x-ray or sigmoidoscopy. How do you feel about that?

Dr. Enquist:—I don't know about the familial history. There was a recent paper from Utah*, I believe, which indicated that the isolated polyp of the colon showed a definite familial incidence.

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*Woolf, Charles M., Richards, Ralph C. and Gardner, Eldon J.: Occasional Discrete Polyps of the Colon and Rectum Showing an Inherited Tendency in a Kindred. Cancer **8**:403, (1955).

I don't know that there is evidence in the literature that there is familial incidence in carcinoma of the colon, but if I had a patient with frank cancer of the colon, and also another polyp elsewhere in the colon, by x-ray, I would be prepared before surgery to do a subtotal colectomy.

Dr. Fierst:—In the remaining ten minutes before the question and answer period, I thought we would touch on ulcerative colitis, which has been discussed very ably this afternoon and, again, I want to ask a question of Dr. Fitzgerald.

What do you think of the pseudopolyp as a precursor of carcinoma in ulcerative colitis, and, also, why do you think—and this is a hypothetical question, perhaps, or a theoretical one—why do you think patients with ulcerative colitis have a greater tendency to form carcinomas?

Dr. Fitzgerald:—I wish I knew the answer. Being a pathologist and thinking very simply about things, this to me represents merely another example of an association somewhat analogous to the increased incidence of carcinoma of the thyroid in hyperthyroidism, adenomas of the thyroid, and in goiter as compared to the incidence of the thyroid cancer in normal thyroid glands. I don't think that the hyperplastic areas *per se* need necessarily be the forerunners of cancers nor that the cancers arise from them.

Perhaps the best explanation is the old one that in hyperplastic or hypertrophied cell populations there is speeding up of metabolism, there is a greater turn-over of cell generations, per unit time, and there is a greater likelihood of the mutant or bizarre cells that we call cancer cells, coming to the fore.

That is an oversimplification by a pathologist, but you asked for it.

Dr. Fierst:—You avoided my question, to a certain extent.

The statement is frequently made in surgical literature that in the presence of pseudopolyposis there is an indication for colectomy. Such notable pathologists as Otani have made the statement that the carcinoma does not arise from a pseudopolyp. Now, it is possible that the patient with ulcerative colitis has the same incidence of adenomatous polyps, as the general population. These polyps are then subjected to the strain of ulceration and healing of the diffuse ulcerative colitis. Therefore, they are more prone to undergo metaplastic changes and become carcinomatous. Can this be the factor which produces carcinoma, or have you seen in your pathological studies carcinoma actually arising in the wall of the degenerating mucosa of a pseudopolyp, with granulation tissue?

Dr. Fitzgerald:—Whether you regard it as a "toxic action" or a "hyperplastic action" is probably irrelevant to the actual process occurring. My point was that the changes may merely accompany the carcinomatous change and may be related to it only *pari passu*. I have not seen cancer arising in such an area.

Dr. Fierst:—Dr. Mellins, is there any way radiologically of differentiating a pseudopolyp from an adenomatous polyp?

Dr. Mellins:—I don't know any way.

Dr. Fierst:—I think it is coming pretty close to five o'clock, and now we have several questions which have been placed before us. Are there any others? These have been addressed to specific speakers on the panel, and I will ask Dr. Enquist to begin, starting from left to right.

Dr. Enquist:—I will try to shorten this question, because it is a long one, but it is about a 60-year old man in otherwise good physical condition, who had or has diverticulosis limited to the splenic flexure and descending colon, none demonstrable in the rectosigmoid. He had these for ten years. Recently he had severe hemorrhage, requiring six blood transfusions. Further study has failed to show any other possible site for the bleeding.

Now the problem is: in a 60-year old man, with long-standing diverticulosis coli, and one incident of severe hemorrhage, and no definite indication of coexisting malignancy, should an elective partial colectomy be done?

I certainly would. I went over a series of 76 patients with diverticulitis at one time, to find out the incidence of gross bleeding, and 3 of the 76 presented with severe bleeding from the rectum. The x-ray and other studies had not revealed any other lesions so we assumed they had bled from the diverticulosis and diverticulitis. A study of the 76 patients showed that frank gross bleeding per rectum was noted in 10 per cent, although it was severe in only 3. So, in a man who has bled so severely and with definite diverticulosis, I would not hesitate to resect him from the midtransverse colon to the rectosigmoid junction, and carry out an end-to-end anastomosis.

Dr. Mellins:—I think both of these questions can be answered at one time:

1. What do you consider the minimum number of exposures for proper examination of the colon?

2. What are your suggestions for the preparation and what is the technic for adequate air contrast films to detect polyps?

I would not want to answer the first question, regarding the minimum number of film exposures, directly, because I think it helps to put the emphasis in the wrong place. The basic study of the colon by barium enema, as in any fluoroscopic study, is no better than the man doing the fluoroscopy. Any fixed number of exposures is just as unthinkable as putting your sigmoidoscope in postiion in a patient and having your office assistant attach a camera and make a set of photographs in lieu of a careful direct study.

The fluoroscopic study is by all odds most important and cannot be overemphasized. The true minimum number of film exposures would be composed

of those areas which are difficult to see fluoroscopically. This would include the lateral view of the rectosigmoid, a compression film of the cecum, compression spot films of any areas of the colon in which anything suspicious is seen.

I feel that the minimum number of large film exposures which I have used to complement my fluoroscopy would vary from what other people might use to complement their fluoroscopy. I have used one "penetrated" film of the filled colon, one evacuation film, using the tannic acid technic, and one air contrast film.

Now, to answer the second question, as to suggestions on preparation for and the technic of adequate air contrast films. It should be said that the air contrast study I have just described is not the usual one, because the usual one presumes that a preliminary filled study has been done so as not to miss anything in the cecum, and then on another day the patient comes back for the air contrast films.

This has been well described by Morton, and Stevenson, and Robinson, and I will just tell you briefly about it. It involves the use of castor oil by mouth, saline enemas, and an adhesive barium mixture combined with tannic acid.

Dr. Enquist:—You won't get out of it that easily. I will pass one of mine to you, and I recognize there are probably different experiences when comparing the clinical experience with the pathological experience.

How often do you see perforations of carcinoma of the colon?

Dr. Fitzgerald:—Rarely, today. Let me put it this way: I think perforations of the colon are pretty likely to get into the surgeon's hands first, and they come ultimately, if not sooner, to the pathologist. In clinics which treat patients from the higher economic levels of life I would expect that perforation is less common than in our municipal hospital where our patients usually appear for treatment at a much further advanced disease-stage.

Dr. Enquist:—Well, as probably many of you know, the clinical experience that we are having in our university is at a large New York City hospital with patients who do not come in until they are forced into the hospital. I think we have a relatively higher incidence of carcinoma of the colon than elsewhere; I would still guess that perforation does not happen in more than about 3 to 5 per cent of our patients.

Dr. Enquist:—It is certainly quite rare, even in our hospital clientele.

Dr. Fierst:—Just so that I do not feel neglected, I have two questions here on diverticulitis:

Is there such a thing as diverticulitis, or is it not a sigmoiditis with frequently, also, proctitis?

There has always been associated inflammation of the colon. It is really a pericolitis as well as a sigmoiditis. There may be obstruction of the diverticulum and one can also have intrinsic abscesses in the wall of the colon. There also are frequent mucosal changes. One must recognize that diverticulitis may occur in the right colon less commonly.

The second question referring to this problem is: Is diverticulosis congenital or acquired?

I think one can say it is both. I feel that if one were to differentiate between these, one could say that congenital diverticulosis is a result of the inadequate recanalization of the solid phase of embryonic development in the gut. A double channel is set up and if there is a connection between the two channels a diverticulum or pouch is formed. If there is no connection then one has an enteral cyst. Congenital diverticuli occur mostly on the antimesenteric border.

Most of the diverticula which one sees, however, are acquired and, as one grows older, one is more likely to develop these areas of weakness in the intestinal wall in association with penetration of vessels. They occur mostly on the mesenteric border.

The second part of this question is: how often have you seen acute diverticulitis as the first sign of sudden onset of constipation?

Diverticulitis is associated most often with diarrhea. Occasionally, however, one may see a case of diverticulitis with signs of intestinal obstruction and obstipation. I would think that is fairly rare. I can't think of more than two instances, offhand.

Dr. Enquist:—Wait, now! We probably see more than you because we often see the old derelict patients who come in with a red hot diverticulitis, especially ruptured diverticula with peritonitis. You are excluding that in the discussion.

Dr. Fierst:—There you will begin to have the problem of paralytic ileus associated with peritonitis.

Dr. Enquist:—It is so. We see ileus in the high percentage of the patients we are called upon to study and treat.

Dr. Fierst:—With peritonitis as a cause.

Dr. Enquist:—Yes.

Dr. Fierst:—One should emphasize, however, that as a general rule, in practice the milder case of diverticulitis starts with a diarrhea.

Dr. Enquist:—I have a question here:

Would you resect an acute diverticulitis even when a relative obstruction is present?

It all hinges on the significance of the word "relative". I think the point that the doctor is making is a good one, and one can never emphasize too much that the obstructed colon does not do well if divided and anastomosed. We can get into the small intestine readily in these days, particularly since we have the antibiotics, but in obstruction of the colon, which is a thin-walled viscus, the risk of breakdown is great.

There is a subsequent question:

Do you not always have a certain degree of obstruction present in cases of acute diverticulitis?

Yes, certainly, one has. With the swelling of the bowel wall there is relative obstruction in all these cases, but if one is operating on them and the degree of obstruction is not great, we will go ahead and do a primary resection.

I have another question:

What do you recommend as adequate treatment for the polyp that is accessible by the sigmoidoscope?

As far as I am concerned, complete removal and fulguration of the base is satisfactory.

Question:—What advice would you give to a patient with a small polyp with a stalk in the sigmoid beyond reach of the sigmoidoscope?

I personally would do a polypectomy, but this brings up the question which I neglected to answer or discuss before, and it was alluded to by both Dr. Mellins and Dr. Fitzgerald. The sessile polyp is treated differently from the true pedunculated lesion. I think most surgeons lean to doing a primary segmental resection for sessile lesions.

A further question:

In case the x-ray shows inflammatory reaction without pain or temperature, would you do an exploratory laparotomy on the patient, or would you treat this condition with sulfonamides and antibiotics for three or four weeks, and re-x-ray the colon, before you would resort to surgery?

Well, I am perfectly aware, as I said before, that most diverticulitis is never seen by surgeons. It is seen by the general practitioner and internist, who is tiding the patient over, and therefore in a diverticulitis in which there is no pain, and in which there is no fever, one has a hard time to convince the patient that a resection is indicated, and a hard time even to convince the doctor unless cancer cannot be ruled out. So, I would go along with most doctors and say they do not require a primary resection although for long-term treatment it may be the most favorable method:

Question:—Suppose you resect a colon for ulcerative colitis or diverticula due to diarrhea for years, with bleeding, and about a week later the individual has a hemorrhage from the rectum. Two weeks after the operation, you explore again and do another resection and anastomosis, and about four weeks after this second operation the patient still has hemorrhages, what would you look for and suspect as the cause of the bleeding?

Well, here we get down to the surgical treatment of ulcerative colitis, and I personally feel that not enough patients with ulcerative colitis are being treated surgically. The proper treatment for ulcerative colitis is pancolectomy, including the rectum, with a terminal ileostomy.

Cattell has made the statement that 33 per cent of the patients he has treated for ulcerative colitis (and he has a large surgical experience) who had the disease for nine years or more had a carcinoma in the colon. That is a very high incidence. Dr. Clarence Dennis found the following incidence: If the patient had a history of less than 10 years, none of his patients had a carcinoma; if they had ulcerative colitis for 10 to 20 years, 10 per cent had a carcinoma in the resected specimen; if they had ulcerative colitis for 20 years or more, 20 per cent of the patients had a carcinoma in the resected colon. So I think that as cancer prophylaxis, more colons should be resected for ulcerative colitis.

Dr. Fierst:—The hour is growing late, and I think we have answered or tried to answer all the questions.

I want to thank the members of the panel and all of you for staying with us this long.

ROENTGEN EXAMINATION OF THE ESOPHAGUS*

BERNARD S. WOLF, M.D.†

New York, N. Y.

In recent years, there has been a remarkable increase in clinical interest in diseases of the esophagus particularly in benign inflammatory conditions asso-

Fig. 1—A mild peptic esophagitis in a patient with a small concentric or sliding type of hiatus hernia and a duodenal ulcer. This combination is quite frequent and of special clinical importance. Under such circumstances, it is necessary to demonstrate the maximum degree of distensibility of the esophagus proximal to the hernial sac because lack of distensibility in this area is the best sign of the presence of inflammatory changes. In this case, over a distance of about 3 cm. proximal to the hernial sac, the esophagus shows limited distensibility. There is no evidence of any filling defect and the junction with the normally distensible esophagus proximally is smooth and tapering. It is very difficult to demonstrate the mucosal pattern in the narrowed area. The amorphous appearance of the barium may suggest inflammatory changes but in such instances there is no discrete ulceration or projecting ulcer pocket.

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†Director, Department of Radiology, The Mount Sinai Hospital; Associate Clinical Professor, Columbia University.

ciated with hiatus herniae. An intensified effort has also been made to discover lesions of the esophagus before they become completely obstructive (Figs. 1, 2). As a result, the methods of examination of the esophagus have had to be refined or amplified and special procedures or maneuvers designed to demonstrate such

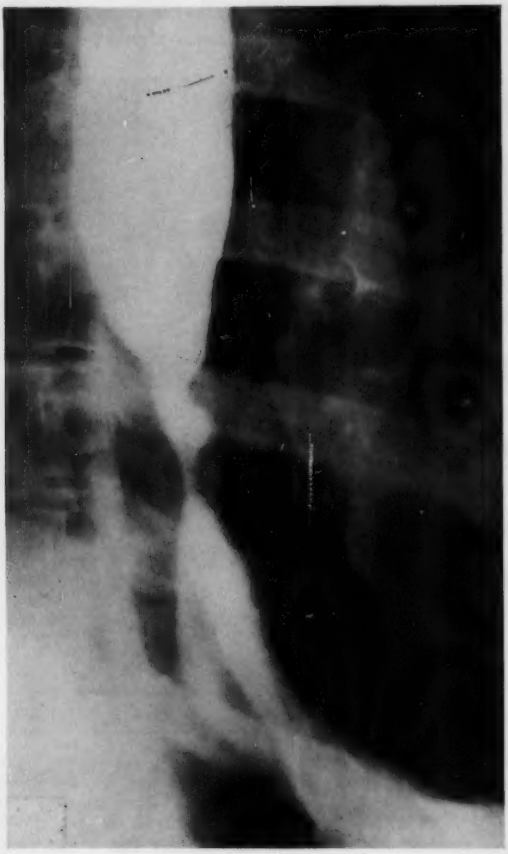

Fig. 2—This is an example of a discrete ulceration of peptic character in the distal portion of the esophagus immediately proximal to a small hernial sac. The terminal portion of the esophagus in the region of the ulceration shows limited distensibility both proximal and distal to the ulceration. In the early stages, such narrowing apparently is the result of mucosal and submucosal inflammatory exudate as well as spasm but in the later stages it may become fibrotic.

lesions. To some extent, the roentgen examination of the esophagus has been neglected because it is so easy to include a few fleeting observations of this viscus as part of a so-called gastrointestinal series. Moreover, when a specific

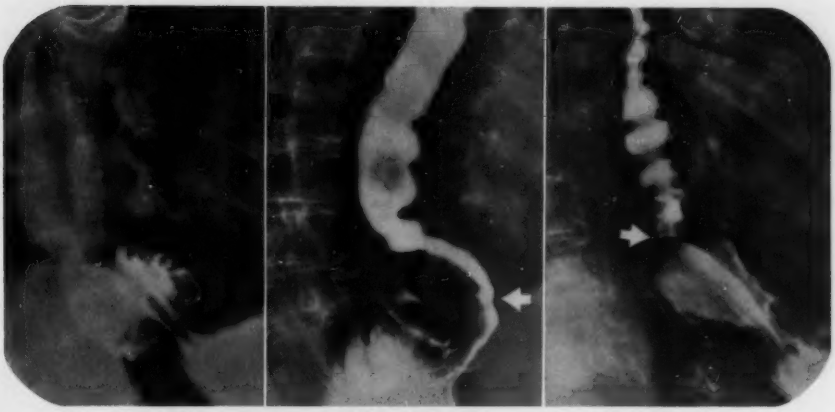

Fig. 3a Fig. 3b Fig. 3c

Fig. 3 —A patient with a moderate size hiatus hernia.

Fig. 3a—The hernia is well visualized but there is no barium in the esophagus so that the status of the esophagogastric junction cannot be determined.

Fig. 3b—Left oblique view of the lower end of the esophagus and proximal portion of the stomach with the patient swallowing barium continuously suggests that the distensibility of the distal esophagus is limited.

Fig. 3c—Same patient in the right oblique projection confirms the fact that the terminal portion of the esophagus does not distend normally and shows marked so-called curling or multiple tertiary contractions in the distal esophagus. In many such instances the fact that the distal end of the esophagus is limited in distensibility particularly immediately proximal to the hernial sac will not be detected unless films of maximum filling are obtained with fluid-barium and unless multiple projections are utilized.

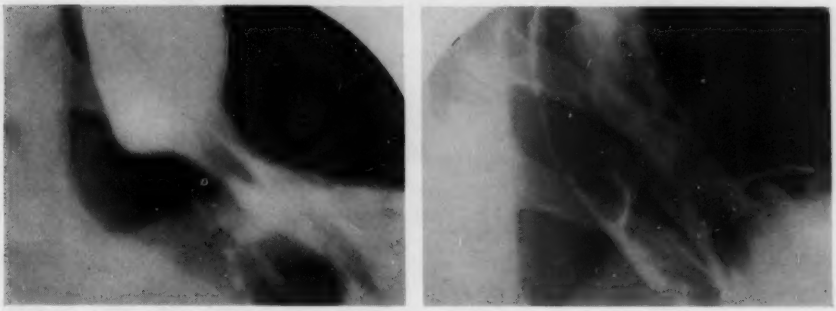

Fig. 4a Fig. 4b

Fig. 4 —Spot views of the region of the hiatus in a patient who had had a subtotal gastrectomy for ulcer.

Fig. 4a—Shows the appearance in moderate inspiration which does not look particularly remarkable.

Fig. 4b—During the course of examination, it was evident that the region of the hiatus rather suddenly became extremely wide indicative at least of so-called "hiatal insufficiency".

request was made for examination of the esophagus *per se*, the examination was frequently conducted by using thick barium preparations. It is not clear why this method of examination of the esophagus became established practice but it must be assumed that it was resorted to because of the fact that the usual fluid-barium mixture traverses the esophagus so rapidly that observations may be difficult to make. It is now evident, however, that for the large majority of lesions, the best method for the examination of the esophagus is to use a fluid-barium mixture of the same consistency used for the routine filling of the

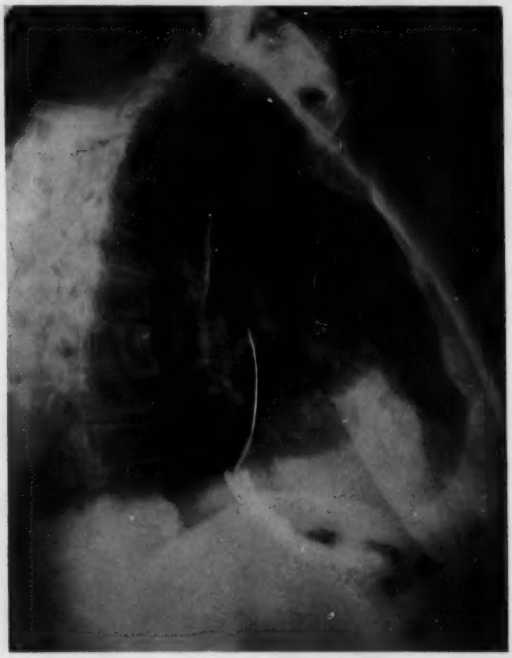

Fig. 5—"Double contrast view of the esophagus" shows limited distensibility over a segment about 2¾ inches in length which actually is located proximal to a sliding hernia and is a residual of peptic esophagitis.

stomach in order that the distention of the esophagus can be tested and that contours of the filled esophagus can be studied (Fig. 3). The administration of thick barium does not distend the esophagus in any regular fashion and the barium paste usually sticks to itself rather than to the esophageal wall creating a variety of bizarre purely random appearances. It is not recommended that thick barium be abandoned completely in the examination of the esophagus since it is of particular use for the demonstration of esophageal varices and occasionally for superficial ulceration of the mucosa of the esophagus. The use

of thick barium, however, should never replace the examination with fluid-barium which should be done first. Observations of the transit of fluid-barium through the esophagus are best made with the patient recumbent since to some degree the transit time is increased. When an obstructive lesion is present, however, so that barium is retained proximal to the site of obstruction, the erect position is, usually more useful since the column of barium, which builds up proximal to the site of obstruction, will also serve as a source of pressure to push barium through the narrowed area. Moreover, under such circumstances air is usually swallowed as well as barium and it may be difficult to get satis-

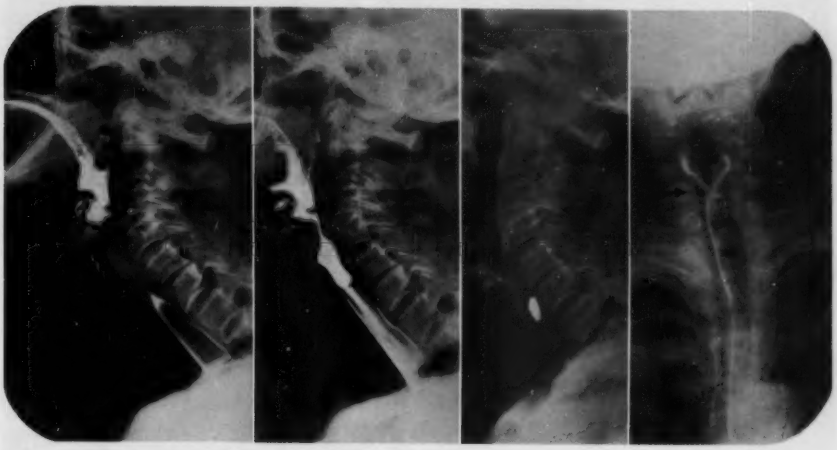

Fig. 6a Fig. 6b Fig. 6c Fig. 6d

Fig. 6 —Patient with a web at the cricopharyngeal region. These films were taken with the patient erect in the direct lateral projection.

Fig. 6a—This type of filling is usually obtained when the patient does not drink continuously. The entire hypopharynx is contracted and the presence or absence of a lesion cannot be ascertained.

Fig. 6b—With persistence, complete filling can usually be recorded and in this instance demonstrates a web at the entrance of the cervical esophagus. Incidentally, the jet of barium traversing the web and entering the cervical esophagus is well demonstrated.

Fig. 6c—Shows the fact that an opaque pill was persistently obstructed at the cervical esophagus. Obstruction to an opaque pill ½ inch in diameter such as this is also indicative of the presence of a stricture.

Fig. 6d—Demonstration of the web in the PA projection confirms its circumferential nature.

factory filling of a partially obstructive lesion with the patient recumbent. Despite the use of the recumbent position to observe the transit of fluid-barium mixture through the esophagus, in the absence of obstruction, this occurs so rapidly that it is often necessary to use the spot device to obtain satisfactory films. In general, spot devices are now easily available and their use is considered an integral feature of the examination of the stomach and duodenum. The same spot device functions quite well for radiographs of the esophagus.

For this purpose, the compression cone of course is not utilized. Instead, it is convenient to cut out a rectangular aperture which can be brought into place so that more than one exposure of the esophagus can be made on a single film. If the long axis of this aperture is in the direction of the long axis of the esophagus, a considerable portion of the esophagus can usually be obtained on a relatively small film. For studies of the region of the hiatus itself, the more frequently used four-on-one aperture is sometimes quite satisfactory (Figs. 4a and 4b).

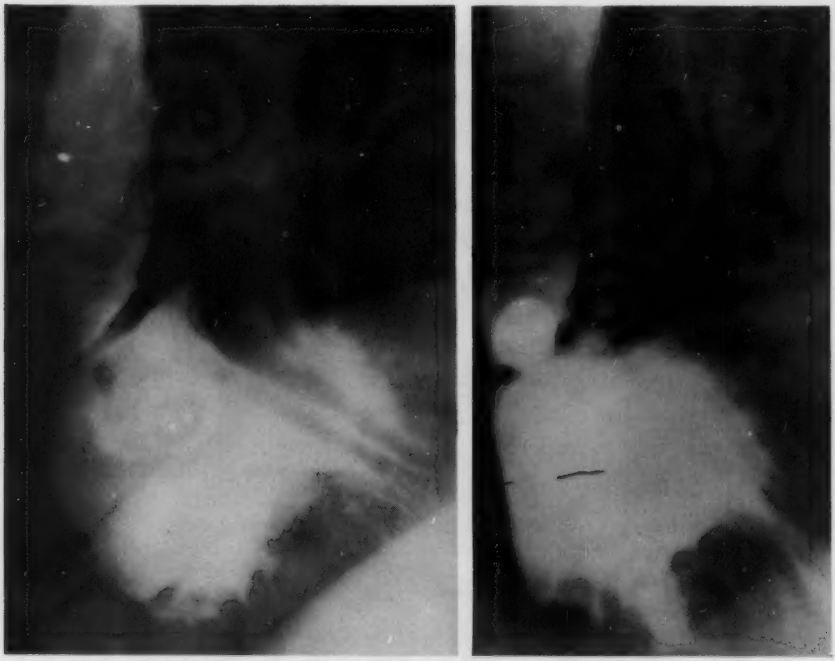

Fig. 7a Fig. 7b

Fig. 7 —Patient with a hiatus hernia and a narrowed esophagogastric junction.
Fig. 7a—Shows the ring appearance which can be demonstrated if the area is maximally distended with air and barium.
Fig. 7b—An opaque pill ½ inch in diameter does not pass through the narrowed ring. The size of the ring is easily determined by comparison with the known size of the opaque tablet.

With the patient recumbent, the most useful position to examine the esophagus is with the patient prone and the left side moderately elevated. The esophagus can then be seen between the cardiac shadow and the dorsal spine and the left leaf of the diaphragm is relatively low. The supine position of the patient with the right side somewhat elevated is, in general, not as satisfactory because the left leaf of the diaphragm is then at a relatively higher level. When

a nonobstructive lesion is found, an effort should be made to demonstrate it in both obliquities as well as the AP and lateral projections. It is true that in order to accomplish this in many instances with fluid-barium, it is necessary to coax the patient to drink the required volumes. In some patients particularly children, this may be quite difficult and it may be necessary to repeat the examination on a subsequent day in order to complete the picture. It probably need not be emphasized that in the case of the examination of children, food should be withheld so that the child comes to the examination in a hungry state. In the case of adults, if the examination is exclusively of the esophagus, this presumably is not necessary but since it is difficult to anticipate in advance in many cases whether the lesion is going to be in the distal esophagus or the proximal portion of the stomach, it is wise to have even adults appear in a

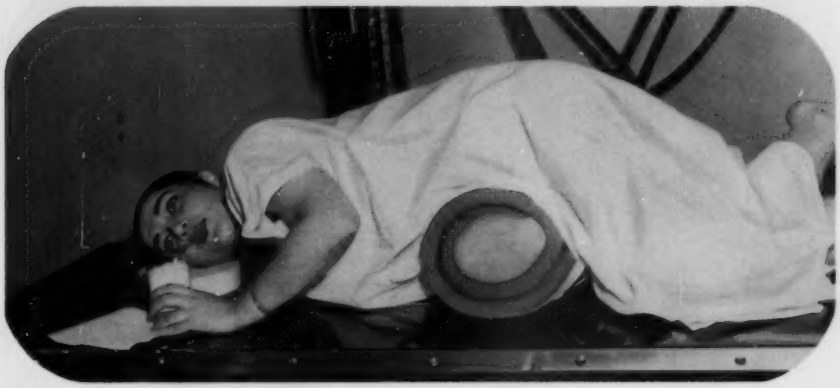

Fig. 8a—The position of the patient for the routine film of the esophagus and upper portion of the stomach. The patient is in the so-called right anterior oblique position. The table is horizontal so that there is no difficulty in placing the glass of barium on the table and having the patient drink through a straw. A radiolucent mat is rolled up and placed underneath the abdomen of the patient so that intraabdominal pressure is increased relative to intrathoracic pressure. The tube is tilted towards the feet and the patient is directed to drink rapidly and continuously.

fasting state. Observations of the esophagus in multiple obliquities as well as the PA and lateral projection are particularly important in the investigation of extrinsic pressure defects on the barium column, for example, by anomalous vessels. Under such circumstances, it is important to include a perfectly straight PA and a perfectly straight lateral projection. Such straight PA and lateral projections are also important in the examination of the cervical esophagus and the pharynx. Oblique views of the barium passing through this region are often difficult to interpret so that in general such oblique views should be taken in pairs with both a right and left obliquity at the same angle. In examination of this area, it is also important that the head not be twisted on the neck so that the passage of barium will be as symmetrical as possible. For this reason, the

recumbent position for the pharynx and cervical esophagus is often less satisfactory than the erect position in which twisting of the head can usually be prevented.

It is often suprising to note how much air patients swallow while drinking fluid-barium mixtures not only at the beginning and the end of such a swallow but during the course of swallowing. This is not abnormal and no special significance can be placed upon it. The fact that this occurs, however, can often be taken advantage of in efforts to get "double contrast" views of the esophagus with air and barium. For example, after the patient finishes a glass of barium through a straw in the recumbent position, she may be directed to continue

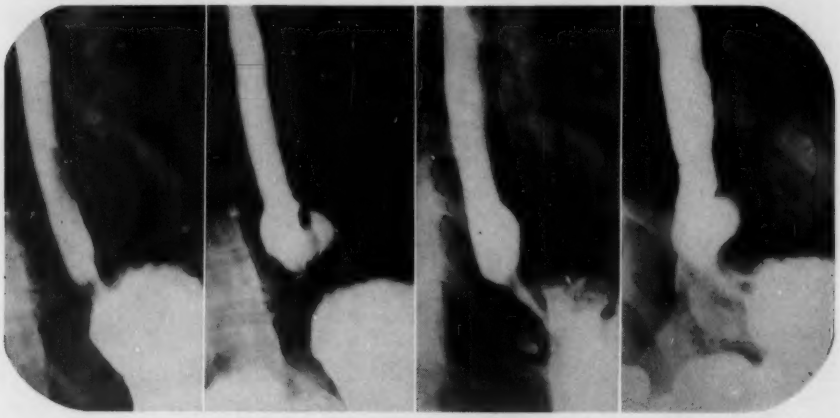

Fig. 8b Fig. 8c Fig. 8d Fig. 8e

Fig. 8b—In this patient in the right anterior oblique position swallowing fluid-barium but without pressure on the abdomen, there is no evidence of a hiatus hernia.

Fig. 8c—In the same patient as shown in 8b with pressure on the abdomen, a definite hernial sac is demonstrated.

Fig. 8d—In another patient without pressure on the abdomen there is no definite evidence of a hernial sac.

Fig. 8e—Same patient with pressure on the abdomen demonstrates a wide hiatus with a hiatus hernia.

to drink, despite the fact that the glass is emptied, and instructed to swallow air. The pressure of an air column in the esophagus is uniformly exerted so that areas of relatively limited distensibility can be easily discerned (Fig. 5).

In instances where there may be only a moderate narrowing in some portion of the esophagus which may be difficult to ascertain because of the rapid flow of barium, the presence of such narrowing may be unequivocally demonstrated by the use of a compressed barium tablet of standardized diameter. We have utilized for this purpose a tablet about ⅜ inch in diameter which has flattened sides so that it is easy to swallow. The diameter of ½ inch corresponds

to a 36 French esophagoscope. If such a tablet can be swallowed and traverses the esophagus without difficulty, one can be fairly certain that no stricture is present which would be a cause of dysphagia. There are two regions where the use of such a tablet is most useful, the first at the upper end of the esophagus for the demonstration of webs (Fig. 6) and the second at the lower end in the presence of a hiatus hernia to detect narrowing in the region of the

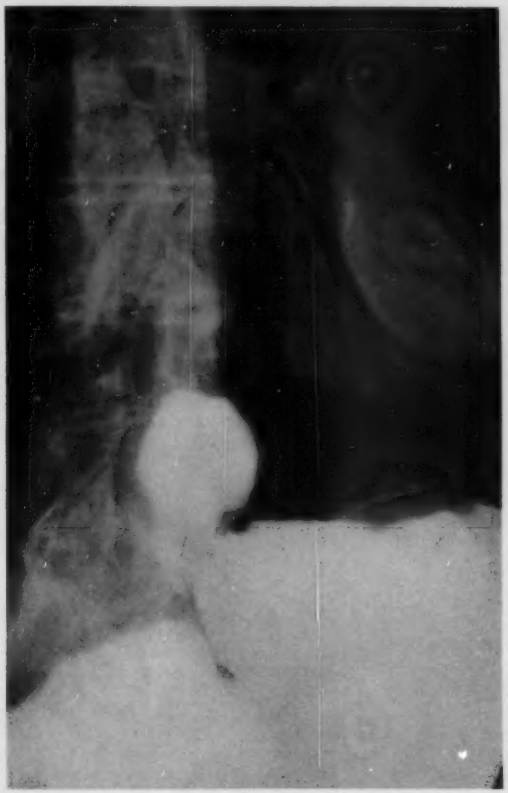

Fig. 9—Patient on her back in a moderate Trendelenburg position showing reflux of barium from the stomach into a small hernial sac. None of the barium has entered the esophagus.

esophagogastric junction (Fig. 7). When a pill such as this is obstructed in the hypopharynx or cervical esophagus, it is usually regurgitated after a short interval. When it is obstructed at the esophagogastric junction, it disintegrates under the influence of the secretions over a period of about 15 or 20 minutes. The circular shape of the tablet prevents it from obturating a site of stenosis

so that actually obstruction is not increased even though the tablet is prevented from passing. Incidentally, the fact that the tablet is of a standard size makes it simple to estimate the exact caliber of stenotic sites since the magnification factor is automatically obtained by measuring the diameter of the tablet on the available film.

As regards the subject of hiatus hernia, the radiologist has the problem, 1. of demonstrating small herniae and 2. of searching for the presence or absence of regurgitation of gastric contents into the esophagus. We have found that

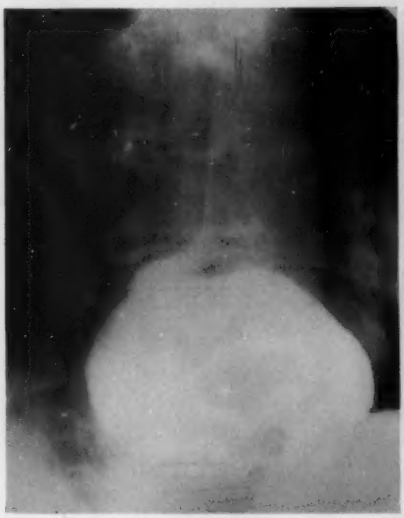

Fig. 10a

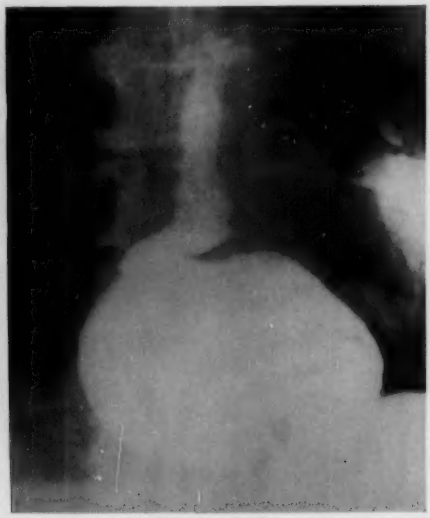

Fig. 10b

Fig. 10 —Patient with a moderately sized direct type of hiatus hernia in Trendelenburg position with combined Valsalva.

Fig. 10a—Shows a thin stream of barium being pushed into the esophagus.

Fig. 10b—As the Valsalva is maintained, the width of the barium column in the esophagus is increased. In such an instance, there is free regurgitation of barium into the hernial sac but regurgitation into the esophagus required not only the influence of gravity but a maneuver to increase intraabdominal pressure. This therefore does not qualify as "free regurgitation" into the esophagus.

the simplest way to demonstrate a hiatus hernia is to have the patient in the recumbent, so-called right anterior oblique position, and to drink fluid-barium rapidly and continuously. In addition, however, a lucent bolster, for example a rolled up lucent mat, is placed underneath the abdomen of the patient while she is swallowing so that intraabdominal pressure is thereby increased. If this is done, maximum herniation and maximum distention of the esophagus can usually be achieved. It may require some practice to have the patient drink rapidly and continuously but, if she will, it is not necessary to instruct her to

hold her breath during the taking of the film since breathing automatically ceases during swallowing. It is true that placing a radiolucent bolster underneath the abdomen produces a moderate degree of the Trendelenburg position which, however, is not as important as the increased pressure applied to the abdomen. The central ray is tilted somewhat towards the feet, i.e. perpendicular to the dorsal spine and a 14 x 17 film will usually include the intrathoracic portion of the esophagus as well as the upper part of the stomach. Figure 8 shows the position of the patient for this film, which is taken routinely as part of each so-called gastrointestinal series, and also demonstrates small herniae which can easily be detected by this method in contrast to the films taken without pressure on the abdomen.

A large number of maneuvers have been recommended for the demonstration of reflux of barium from the stomach into the esophagus. It is questionable

Fig. 11—Patient is in the "Johnstone position" that is the patient is erect but bending over as if to touch his toes. The hernial sac is seen on the right within the shadow of the diaphragm and barium is refluxing and filling the esophagus. This position is not satisfactory unless the stomach has been previously well filled with barium and unless the patient can bend over sufficiently far so that the plane of the esophagus is below the fluid level in the stomach.

whether some of these more strenuous procedures such as applying a pressure cuff around the abdomen and blowing it up until the patient cannot tolerate it any further are of clinical usefulness. It would seem that under such circumstances reflux could be produced in many individuals but that it would have no clinical significance. We therefore prefer a more modest test by placing the patient in a moderate degree of Trendelenburg position, face up, which serves to displace the barium to the fundus of the stomach and which will usually fill a small hernial sac if reflux occurs freely. In this connection, it is important to note that while a hernial sac is commonly filled (Fig. 9), in many instances the barium does not reflux into the esophagus *per se*. If with the

patient in this Trendelenburg position, a Valsalva maneuver is also performed, some barium may be actively pushed into the esophagus (Fig. 10) but it is still evident that it is not occurring freely under the simple influence of gravity. It is therefore important in reporting the presence of regurgitation to indicate under what circumstances it was demonstrated. Another position or maneuver which we utilize frequently for the demonstration of regurgitation is the so-called Johnstone position (Fig. 11) which is performed with the patient standing and is therefore convenient during vertical fluoroscopic examination. In this maneuver, the patient is asked to bend over with his hands forward as if to touch his toes so that the level of the esophagus is brought below the level of the barium in the stomach and, simultaneously, the jackknifing of the abdomen serves to increase intraabdominal pressure. The patient is viewed in the lateral projection while he is bent over to determine whether barium refluxes into the esophagus. Again, reflux may occur very rapidly and promptly and fill the esophagus in a continuous column or it may be forced to leak into the esophagus by combining the Johnstone with a Valsalva or Müller maneuver. Although the Johnstone position when it is well done is a more severe test for regurgitation than the simple Trendelenburg position, it nevertheless appears to be a reliable indication of clinically significant regurgitation. Of course, the fact that a sac can be filled during regurgitation in either the Trendelenburg or Johnstone positions is also indicative of the presence of a hernia. In fact, the blown-up saccular configuration is more often obtained under conditions of reflux than during regular swallowing. It should be emphasized, however, that with simple tests for regurgitation such as those described above, the absence of regurgitation during the course of a particular examination does not exclude the presence of a hiatus hernia. In fact it is well known that regurgitation may not be demonstrable during the course of a particular examination and be easily demonstrated at some later occasion.

Discussion

Dr. O. H. Wangensteen:—My role as surgical discussant here is somewhat difficult to evaluate inasmuch as the only paper concerning the esophagus is this one on diagnosis. I do want to compliment Dr. Wolf on the pains he has taken to demonstrate lesions of the esophagus. The esophagus has not often been the subject of special study by gastroenterologists who profess an interest in radiology, as Dr. Wolf pointed out.

I brought a few pictures along which depict some of my own interests in lesions of the esophagus. I will start by commenting briefly on one of Dr. Wolf's pictures. Dr. Wolf alluded to the presence of ectopic gastric mucosa—an occurrence which certainly every surgeon evincing an interest in the esophagus has seen. In my own experience, however, gastric reflux has been a far more common cause of esophageal stricture. In my clinic, as many of you know, we have treated idiopathic strictures of the esophagus by gastric resection with consid-

erable success over a period of many years. In fact the first patient was done in September 1939. This first patient had been treated in our clinic for esophageal stricture for 4 years, and during that interval had undergone more than 100 esophageal dilatations. The gastric resection, undertaken for massive gastric hemorrhage from a duodenal ulcer cured the stricture. The patient reluctantly underwent 2 dilatations in the first 2 months following gastric resection, but said he then could swallow very well without esophageal stretching. I have spoken of these cases often in these discussions. In 1949 when the first report was made, [*Surg., Gynec., & Obst.*, **88**:560-570, (May), 1949] we had seven cases—many of them were truly remarkable. One patient with a long and very narrow stricture of the esophagus had carried a gastrostomy for eight years because he could not swallow his saliva. More than eight years have gone by since he underwent gastric resection, and today he can eat meat, celery, carrots, hard rolls and other such items which are notably difficult for patients with esophageal stricture to swallow. Dr. MacLean of this Clinic reported earlier this year an enlarged experience with this method of treating idiopathic esophageal strictures [*Surg., Gynec., & Obst.*, **103**:5-14, (July), 1956]. The results are good and we are enthusiastic over the method. It certainly is far simpler than esophagogastrectomy with excision of the stricture. There have been no failures. An esophageal bougie is passed three weeks after operation and again at 6 weeks, if there is any difficulty in swallowing. The stricturing process in reflux esophagitis goes only to the circular muscle. Prevention of reflux and a few dilatations in the early postoperative period insures restitution of a fairly normal esophagus.

Resistance to the idea that so-called idiopathic strictures of the esophagus are really acid peptic in origin has gradually died out with demonstration of the great sensitivity of the esophagus to injury by the digestive juices, and especially by acid peptic juice. When in 1944, after two operative successes (1939 and again in 1942 in a second patient), the speaker proposed applying gastric resection (including provision for adequate gastric drainage) to a corkscrew-like stricture at the juncture of the middle and lower third of the esophagus, the suggestion met with no suggestion of acceptance by any members of the Surgical or the Medical Staffs of our University Hospitals. The idea, however, appealed to the patient and the operation proved a great success. This patient too had undergone more than 100 dilatations of esophagus. She was permanently relieved following performance of the gastric resection and two dilatations in the early postoperative period. She survived for more than seven years thereafter and needed no further dilatations. The patient had polycystic disease of the kidneys and liver, of which condition she died, somewhat past the Biblical promise of three score and ten years.

That gastric resection with the addition of provision for adequate gastric drainage will overcome the difficulties of acid peptic stricture (idiopathic stricture) of the esophagus has been well demonstrated in this experience.

Some esophageal surgeons continue to have us believe that hydrostatic pressure is the primary cause of so-called "spontaneous perforation" of the esophagus. Experiments reported by Brackney et al (Brackney, E. L., Campbell, G. S., Thal, A. P. and Wangensteen, O. H.: Spontaneous Perforation of the Esophagus: Experimental Study, *Proc. Soc. Exper. Biol. & Med.* **88**:307-310, 1955) sets aside quite definitely that thesis too, in that pyloric obstruction failed to produce perforation of the esophagus attending the administration of histamine following excision of the acid peptic area of the stomach.

In our clinic, hiatal hernia is repaired through a lower sternal splitting incision, cutting out into the fourth intercostal space, complemented with a midline upper abdominal incision. This incision provides wonderful access to the attic of the abdomen. The surgeon cuts the diaphragm in the midline until the pericardium comes into view. If the surgery of access is still not adequate, he may either incise the fibrous pericardium or both layers of the pericardium, thus providing maximal exposure. The subdiaphragmatic esophagus is elevated on a tape; the esophageal crura of the diaphragm are defined, and these are sutured to one another, thus narrowing the orifice about the esophagus. Finally, a few coaptation sutures are placed between the subdiaphragmatic esophagus and the peritoneum adjacent to the diaphragmatic crura. It is the surgical exposure which makes this a very easy and simple operative procedure.

In speaking of the esophagus, it is quite proper, I believe, to mention that we employ the esophagus of the cat now quite routinely in trying to assess the potiential digestive capacity of gastric juice. This technic (Perry, John F., Jr., et al: Digestive Action of Human Gastric Juice, *Proc. Soc. Exper. Biol. & Med.*, **92**:237-240, 1956) provides an excellent means of assessing the potential digestive capacity of the gastric juice in a number of conditions. The digestive juice possesses great digestive power in duodenal ulcer as contrasted with gastric ulcer. In fact the dripping of gastric juice obtained from patients with duodenal ulcer will cause perforation of the cat's esophagus in approximately 25 per cent of instances; the majority of the remainder will present evidences of severe esophagitis; the juice obtained from patients with gastric ulcer practically never exhibits any evidence of digestive action upon the cat's esophagus. It can readily be demonstrated also that the digestive power of the gastric juice of patients with intact normal stomachs is enhanced after aggressive abdominal operations. The same is true of other stresses such as burns. This technic of esophageal perfusion assessment of the digestive power of gastric juices also has been found useful in appraising the likely success of operative procedures in protecting against recurrent ulcer. It would appear that the digestive power of juice aspirated from the stomachs of patients who have undergone previous operations for duodenal ulcer is least in patients upon whom segmental resection was done—another bit of factual information which attests to the superiority of segmental gastric resection in the management of duodenal ulcer.

MEDICAL MANAGEMENT OF PEPTIC ULCER*

CHARLES A. FLOOD, M.D.

New York, N. Y.

In the medical management of patients with peptic ulcer a number of important problems are encountered very frequently. New remedies for ulcer are proposed at frequent intervals and require careful evaluation. In patients with a gastric ulcer which seems benign, the possibility of malignancy must be ruled out. Ulcers of the stomach or duodenum which recur with more than average frequency or which are associated with complications, require considered judgment as to whether there should be surgical intervention. The purpose of the present report is to summarize certain data which seem useful in the approach to these problems.

The immediate objective of medical therapy is the healing of the ulcer crater. The healing time of a crater in the stomach in patients who respond to standard conventional therapy averages about six weeks[1]. There are, however, wide variations. Some lesions disappear completely within two weeks and other benign ulcers may persist for three months or more. While there is a rough correlation between the size of an ulcer and the rate of healing, nevertheless some small benign lesions heal very slowly. In contrast, some larger ulcers, more than 2.5 cm. in diameter, may disappear within a relatively short period of time. The rate of healing of a gastric ulcer is most conveniently determined by serial radiologic examinations conducted every three to four weeks. Gastroscopic studies have confirmed the fact that the average healing time is about six weeks.

The healing time of duodenal ulcer appears to be of the same approximate duration. Studies of patients with duodenal ulcer who have been subjected to serial x-ray examinations during treatment, indicate that the average time required for disappearance of the crater is about six weeks. Unfortunately, radiologic study of duodenal ulcer is open to the objection that it is often difficult to be sure of the validity of the interpretation of crater shadows.

The efficacy of newly proposed methods of medical treatment may be determined by a study of their effect on the rate of healing of ulcer craters in a series of patients. Certain practical difficulties arise, however, with this approach. The study of the effect of new remedies on patients with gastric craters is limited by the fear that one may be overlooking the presence of malignancy. The evaluation of the healing of a crater in a partially deformed duodenum may be deceptive.

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From the Department of Medicine, The College of Physicians and Surgeons, Columbia University and The Presbyterian Hospital, New York.

Other criteria are helpful in the evaluation of methods of ulcer therapy. The effect of various measures upon gastric physiology is important. Thus, for example, a large number of anticholinergic drugs are now available which inhibit the secretion of hydrochloric acid in some measure, as well as inhibit propulsive peristalsis. An ever increasing number of antacids such as alkalis and absorbing agents are available for use in treatment.

While the secretion of hydrochloric acid is essential in the pathogenesis of ulcer and a program of neutralization therapy seems rational as a method for encouraging healing, certain facts make it apparent that the factor of acid secretion is not all important. Ulcers frequently heal spontaneously without treatment. It is also common experience that minimal doses of antacids and extra feedings—a program which neutralizes very little excess hydrochloric acid, will

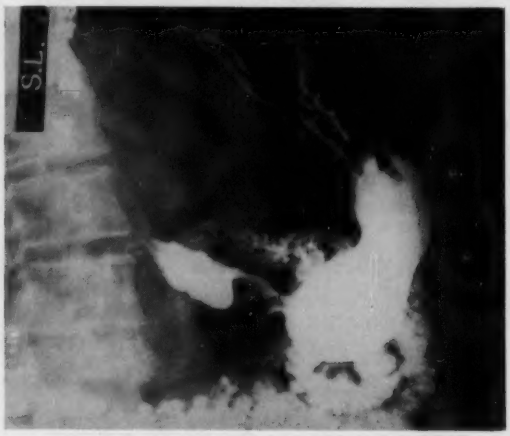

Fig. 1—Benign antral disease. The narrowing of the antrum which was demonstrated radiologically was associated with peptic ulceration of the antrum and duodenum.

result in the healing of many ulcers. The fact that patients with ulcer in the stomach usually do not exhibit hyperacidity also suggests that other factors as yet poorly understood, may be of greater importance than the acid secretion of the stomach. Hence it seems probable that therapeutic measures which are designed to reduce gastric acidity will not be the final answer to the problem of medical treatment.

The evaluation of the efficacy of new methods of therapy proposed for ulcer also rests partly on animal experimentation. A number of animal preparations may be used. These include the ulcer of the Mann-Williamson dog, the ulcers produced with histamine in beeswax and the ulcerations in the stomach of the Shay rat. The value of these experimental preparations as a method of assay is limited and, at times, the results have not correlated well with experience in the treatment of patients.

The ultimate appraisal of remedies for ulcer usually depends on prolonged clinical trial by multiple observers in large series of patients with ulcer. It is useful, however, to have knowledge of their influence upon gastric secretion and motility, their effectiveness in the prevention of experimental ulcer and their influence on healing time in human subjects.

Gastric Ulcer Versus Gastric Carcinoma

The management of the individual with a gastric ulcer is always complicated by the fact that gastric carcinoma can produce a radiologic picture that is identical with that of ulcer. At times the difficulty in diagnosis makes surgical intervention necessary. In some cases it may be problematic whether the chance

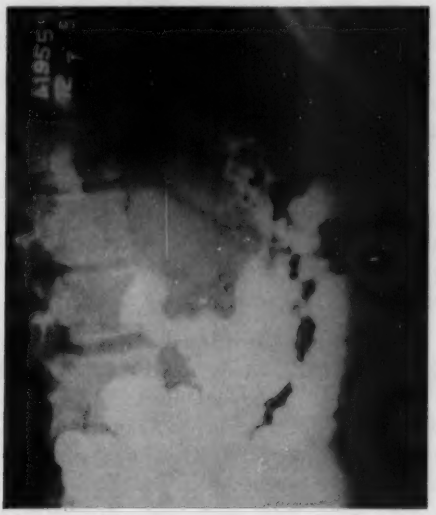

Fig. 2—Malignant antral disease. Radiologic study revealed a crater on the lesser curvature of the antrum. Carcinomatous changes were found in one margin of the ulcer (Case 7).

of curing a malignant lesion justifies the risk of surgery. Many of the patients in whom this problem arises are relatively poor surgical risks.

From the radiologic standpoint, this problem arises most frequently in two types of patient. The first is the patient who is found to have an ulcer crater in the body of the stomach, usually on the vertical portion of the lesser curvature. The other problem is that presented by the patient with evidence of disease in the antral portion of the stomach.

Ulcer craters located on the vertical portion of the lesser curvature or in the anterior or posterior wall of the body of the stomach, as seen on radiologic examination, prove to be malignant in between 10 and 20 per cent of patients.

In a series reported by Smith and Jordan, 17 per cent of such lesions were malignant[2]. Our own experience has been approximately the same—18 per cent of craters in the body of the stomach have been malignant.

If there is not an achlorhydria, one may choose to study the patient further to try to establish a diagnosis prior to consideration of operation. The available methods include cytologic study, gastroscopy and a medical therapeutic trial. Cytologic study and gastroscopic examinations have been helpful, at times, in arriving at an early diagnosis of malignancy. In individual instances gastroscopic examination has revealed evidence which was strongly suggestive of malignancy and it has been possible to avoid a prolonged therapeutic trial.

The test of healing has, in our experience, however, been the most reliable method of differentiation between benign and malignant ulcers in the body of the stomach in patients who secrete hydrochloric acid. Under medical therapy, reexamination of the stomach by x-ray has been carried out at intervals of three to four weeks. More frequent examinations are apt to be misleading because they do not permit sufficient time for healing to occur. If the lesion diminishes to one-half or less of the original size after three to four weeks of treatment, medical therapy is continued until the crater disappears completely. Complete return of the stomach to a normal radiologic appearance has, in our experience, always signified that the ulcer was benign. A considerable number of benign ulcers fail to meet these criteria for healing. It has been deemed necessary to explore these patients for possible carcinoma.

Antral disease with or without evidence of ulceration is the other common radiologic finding in which it is difficult to distinguish between a benign and a malignant process. Benign and malignant disease of the gastric antrum have a number of radiologic characteristics in common. Narrowing of the antrum, crater shadows and irregularities in the contour of one or both curvatures may occur in either condition. In a recent series, benign antral disease as recognized radiologically, was associated with convincing evidence of an old or recent peptic ulcer either in the stomach or duodenum in approximately 80 per cent of cases[3].

We have recently resurveyed a series of patients with benign and malignant antral disease who were originally studied during the period 1947 to 1950[4]. These data are of interest in relation to the policy of management of patients who present this type of radiologic picture. There were 103 patients in the series. The group was composed of a consecutive series of patients at the Presbyterian Hospital who were referred for gastroscopy after radiologic examination had revealed evidence of a diseased antrum. After study, 73 patients were considered to have benign disease of the antrum. The diagnosis was verified by pathologic examination in 27 instances. The impression of benign disease was supported by the record of a benign clinical course for a subsequent period of at least 6 months in the remaining patients.

Thirty of the 103 patients had carcinoma which involved the antrum. This diagnosis was established by operation or by autopsy in all instances. Operation was performed on 29 patients of whom 23 were subjected to gastric resection. A survey of the follow-up course reveals that 7 of these patients survived five or more years. Of these individuals, 6 are still alive at the present time, and 1 patient died with a clinical picture which was attributed to multiple myeloma. The chief findings in these 7 patients with carcinoma were as follows:

Case 1:–Unit #010691–a 45-year old man was first seen in 1950 complaining of epigastric pain of three years' duration. Radiologic examination revealed the shadow of an ulcer crater on the lesser curvature of the antrum consistent with either a benign or a malignant lesion. Gastric analysis revealed the presence of free hydrochloric acid. Gastroscopic examination revealed patches of exudate on the surface of the antrum.

At exploration an ulcer was found which was thought to be benign and a subtotal gastrectomy was performed. Pathologic examination revealed an ulcer extending across the pylorus. Histologically there were two separate areas of malignancy on the gastric side of the ulcer.

The subsequent clinical course has been satisfactory and the patient is well five and a half years later.

Case 2:–Unit #023096–a 43-year old man was admitted to the hospital in 1950 with a five-year history of epigastric pain. X-ray examination showed evidence of a large ulcer on the lesser curvature of the antrum which was thought to be benign in appearance. Gastroscopic examination showed the ulcer to have an irregular margin and there was a small adjacent satellite ulcer–an appearance which was considered suggestive of malignancy. After a trial of medical therapy for approximately one month, a second x-ray examination showed no improvement.

At operation a mass 3 cm. in diameter was found in the antrum and a subtotal gastrectomy was performed. Pathologic study revealed an ulcer with carcinomatous changes in one margin not extending below the submucosa. The patient is alive and well five and one-half years later.

Case 3:–Unit #936846–a 38-year old man was seen in 1949 complaining of abdominal pain of one month's duration. Radiologic study elsewhere had revealed a prepyloric crater shadow and diffuse antral narrowing, which was interpreted as consistent with benign or malignant disease. Gastroscopic examination revealed a large ulceration with irregular margins on the posterior wall of the antrum which was thought to be malignant.

Subtotal gastrectomy was performed elsewhere. Pathologic study showed an ulcerating infiltrating carcinoma with no lymph node involvement. The patient was reported to be well six years later.

Case 4:—Unit #981179—a 56-year old woman was seen in 1950 because of anemia and severe weight loss. Two x-ray studies showed evidence of antral spasm. There was a histamine achlorhydria. Gastroscopic examination revealed atrophic gastritis. Papanicolaou smears of gastric contents were positive for carcinoma.

A subtotal gastrectomy was performed. The specimen contained a carcinoma with a diameter of 1 cm. The lesion did not invade the muscularis. There was no lymph node involvement. The patient is well six years later.

Case 5:—Unit #963020—a 57-year old woman was seen in 1948 with the complaint of anorexia, nausea and vomiting for six weeks. X-ray examination revealed evidence of cholelithiasis and of pylorospasm. At gastroscopic examination a small grayish patch visible at the pylorus was interpreted as retained food.

Exploration revealed both the presence of stones in the gallbladder and of a mass, 2½ cm. in width, at the pyloric ring. Subtotal gastrectomy and cholecystectomy were carried out. The lesion was classified as a fungating and superficial spreading carcinoma.

The follow-up course was satisfactory for five years. Five years after operation the patient became ill and was hospitalized elsewhere. Studies revealed evidence of multiple myeloma and she died of renal failure. An autopsy was not obtained.

Case 6:—Unit #951227—a 73-year old woman was seen in 1949 complaining of substernal burning for four months. Radiologic examination showed an annular filling defect in the distal antrum, characteristic of carcinoma. The stomach contained free acid. At gastroscopy, an ulceration with rolled nodular edges in the antrum was considered to be typical of carcinoma.

Subtotal gastrectomy was performed with the removal of a fungating and ulcerating carcinoma, 5 x 8 cm. in diameter.

This patient is now alive without evidence of recurrence at the age of 80 years.

Case 7:—Unit #024941—a 36-year old man was first seen in 1950 with a history of epigastric burning for one week. On radiologic study a flat ulcer was seen on the lesser curvature of the antrum. Free acid was present on gastric analysis. Gastroscopic examination failed to reveal a lesion although pyloric closure was visualized.

Subtotal gastrectomy was performed and the histologic examination revealed signet ring cancer cells on one edge of the ulcer. There was no lymph node involvement. The patient was well five and one-half years later.

The results of the anteoperative diagnostic studies which had been carried out on this group of 7 patients with a carcinoma which was amenable to surgical therapy, are of interest. Only one patient presented a radiologic picture which was interpreted as showing definite evidence of carcinoma. Four patients presented crater shadows in the antrum which were considered to be consistent with either a benign or a malignant process. The other two individuals presented changes in the antrum which seemed to be benign. Gastroscopic examination revealed convincing evidence of carcinoma in two instances, was suggestive of cancer in one patient and failed to reveal the lesion in four cases.

The pathologic characteristics of the tumors were classified as either those of superficial spreading carcinoma or of fungating carcinoma in six instances. These are the morphologic types of gastric cancer which offer the best prognosis.

The follow-up data on the 73 patients in this study who were considered to have benign antral disease are somewhat incomplete. Sixty-seven patients were examined, however, and were found to be free from clinical evidence of neoplasm, one or more years after the original examination. Five patients were lost sight of in less than one year. One patient, who was considered to have a benign ulcer and cirrhosis of the liver, died elsewhere one and a half years later. The diagnosis in this instance may have been in error.

In summary, in a series of patients with radiologic evidence of antral disease which, in most instances, did not strongly suggest malignancy, approximately 30 per cent had carcinoma, while about 70 per cent had benign lesions. Seven per cent of the entire group were found to have a carcinoma which was successfully treated by means of operation. Since there were only 30 patients in the series who had carcinoma, the five-year survival rate for carcinoma in this small selected group was between 20 and 25 per cent. This figure is striking in view of the fact that the current over-all five-year survival rate for carcinoma of the stomach is approximately 8 per cent in this institution.

In the present series of patients, operation on individuals with a radiologic picture which was entirely consistent with a benign process in the antrum, led to the resection of a number of small carcinomata with a good prognosis. Five of the 7 cancers were less than 3.0 cm. in diameter. Six of the 7 tumors were either of the superficial spreading or fungating variety.

These data favor an aggressive surgical approach in patients with antral disease whenever there is continuing reasonable doubt as to the nature of the underlying lesion.

Long-Term Management of Ulcer

Recurrences may be anticipated in the great majority of patients with ulcer. In the experience of the Follow-up Clinic at The Presbyterian Hospital, the average incidence of recurrences under conservative management has been

approximately once every two years. Of interest is the fact that the recurrence rates recorded in patients with gastric ulcer and with duodenal ulcer were essentially the same (once every 2.4 years and once every 2.1 years respectively)[1,5]. Prompt resumption of treatment with diet and alkalis usually controls the symptoms at the time of recurrence. Patients, therefore, should be instructed to resume such treatment as soon as it becomes evident to them that a recurrence has taken place. In general, the results of this approach to long-term management are reasonably satisfactory.

Less satisfactory results on conservative management may be anticipated in certain groups of individuals. These include patients with intractable pain, patients with the complications of ulcer and some individuals with psychiatric problems.

In our experience an initial slow symptomatic response to hospital treatment is a bad prognostic sign[5]. In a study of patients with duodenal ulcer who had continued to complain of epigastric pain for more than two weeks on ideal conservative management, it was found that the subsequent clinical course was apt to be unfavorable. Such patients were found on follow-up observation to have a recurrence rate of once every 1.2 years, a rate almost twice as frequent as the average.

It is generally agreed that patients with a history of repeated hemorrhage from ulcer have an unfavorable prognosis. A statistical comparison of the clinical course in patients with duodenal ulcer subsequent to a first hemorrhage, with that which followed a second or a third hemorrhage, substantiated this impression. In a group of 253 patients with duodenal ulcer who had sustained one or more hemorrhages, the average incidence of episodes of gross bleeding was once every six years, after the first hemorrhage. After a second hemorrhage, however, the frequency of episodes of further bleeding rose to once every 3.3 years. After more than one hemorrhage from a duodenal ulcer, the risk of further bleeding was almost doubled in this series[6].

There is general agreement that emotional factors play an important role both in the immediate response to treatment and in the long-term outlook in this disease. This was convincingly illustrated by wartime experience with soldiers with peptic ulcer. It was noted by a number of observers that the results of conservative therapy were often less satisfactory than those encountered in civilian life[7,8]. There appears to be a correlation between poor response to treatment and poor morale.

In the long-term management of patients with gastric ulcer the possible development of carcinoma requires continuous vigilance. While the relation of benign gastric ulcer to the development of gastric carcinoma is a debatable question, individual patients who have had an ulcer may, of course, develop gastric cancer. Our own experience lends some support to the belief that there

is a greater tendency for gastric carcinoma to develop in patients who have had a benign ulcer than in comparable groups in the general population. Among 101 patients with benign ulcer followed for an average period of 5.6 years, 5 patients were observed to develop gastric carcinoma from 3 to 19 years later[1].

Summary

1. The effectiveness of medical therapy for peptic ulcer is often difficult to appraise. Observation of the rate of healing of the lesion is probably the most reliable method of assay.

2. A study of patients with antral disease in whom the differential diagnosis between cancer and ulcer frequently remained in doubt, indicated that a considerable number have surgically curable carcinoma.

3. Factors which influence the long-term prognosis in ulcer have been discussed.

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Discussion

Dr. I. Snapper:—I have had plentiful opportunity to convince myself of Dr. Flood's successes in the treatment of gastric ulcer. We must realize, however, that medical treatment of a gastric ulcer in older individuals is actually a therapeutic trial in a disease which has not been diagnosed with certainty. As Dr. Flood has demonstrated, occasionally one is rudely shaken up because a patient with gastric ulcer who, for a long time has been doing well on conservative treatment, all at once is proved to be suffering from a carcinoma. Notwithstanding this objection, however, I fully agree that Dr. Flood has been able to protect an impressive number of patients with ulcer of the stomach from surgical intervention.

Dr. O. H. Wangensteen:—No matter how much Dr. Snapper affects to disagree with me here, I believe, I have had more influence on him than has been apparent in our discussions. (Laughter.) It seems to me that he is leaning a little more to the right than he used to do. In any case, I am glad to hear him say publicly that he now believes in operating on gastric ulcer, not only because the operation removes the lesion, but also because it is now and then an opera-

tion for cancer of the stomach, and that gastrectomy for gastic cancer is a justifiable operation.

Dr. Flood's presentation in which he admits a possibility of a 15 per cent error or chance of being wrong is in general accord with surgical experience. Such an admission does justify a surgeon in taking a rather drastic view in advising operation for gastric ulcer; however, I do not go along with surgeons who suggest that every acute gastric ulcer should be operated upon, and I assume that when Dr. Flood is given the opportunity to respond to this discussion, as he should have in so controversial a subject as ulcer, he will indicate to us which varieties of acute gastric ulcer he believes can be identified as being likely benign and therefore safe to treat medically.

In our own clinic, though surgically-minded, we treat some acute gastric ulcers without operation. Certainly any persistent gastric defect must be treated surgically. A good question is: what is a persistent defect?

Hermon Taylor of the London Hospital visited our clinic at the University of Minnesota several years ago and expressed an interest in visual or gastroscopic control of the healing of acute gastric ulcers. At that time, we had under observation a number of patients who had acute gastric ulcers and who were being treated by bed-rest and a Sippy regimen. Then, after a period of approximately 6 weeks, when the ulcer had appeared to have healed radiographically in all the cases a willy-nilly gastric resection was done to ascertain the fate of the defect, which ostensibly had healed. One of these 13 patients proved to have a cancer, and only one of the remaining 12 had an ulcer which had healed completely microscopically. In the remaining 11, peninsulas of epithelium went out from the edges but a small uncovered erosion or crater could be identified in all. This very circumstance of failure of complete healing undoubtedly is responsible in large measure for ulcer recurrence and usually at the very same site.

In commenting on these observations Hermon Taylor said at that time, "If you had only subjected these patients to gastroscopy before subjecting them to surgery, you probably could have identified the instances in which surgery might have been avoided or postponed."

In the intervening 10 years I have not succeeded in setting up a similar control group with a somewhat longer period of observation and finally subjected to gastroscopy. Patients in my experience do not welcome gastroscopic examinations. I hope in the future someone will repeat these observations with gastroscopic controls. It has been suggested to me that 12 weeks is a better interval than 6, during which to expect complete healing in an acute ulcer. Both periods are too long, however, should the lesion prove to be a cancer.

In any case, with a 15 per cent margin of being wrong on the basis of preoperative considerations surgeons are fully justified in taking a somewhat aggressive attitude toward the gastric ulcer problem. In the cases Dr. Flood cited,

he indicated no real harm had been done by the conservative period of controlled observation and treatment.

Now, with reference to the surgical management of gastric ulcer, excisional therapy is in order. If the ulcer is high on the lesser curvature (a frequent site), in our clinic a segmental resection is performed. The excised specimen is given to the pathologist, who, together with the surgeon, inspects the opened specimen. A frozen section is done, and if the impression of benignancy is confirmed, segmental resection is completed. Such an operation is acceptable also for the so-called juxtacardiac ulcer in most instances. For the antral ulcer, obviously a type of Billroth operation must be done.

As all surgeons are aware, the permanent cure of a gastric ulcer is more readily accomplished than that of a duodenal ulcer. In other words, the stumbling block for proposed operations for peptic ulcer has stemmed largely from the surgeon's ability to cope as readily with duodenal ulcer as with gastric ulcer. Recurrent ulcer, after an adequate resection for gastric ulcer, is virtually unknown. There is, however, a definite recurrence rate following the Billroth II gastric resection for duodenal ulcer, probably ordinarily in the area of 3 to 5 per cent, depending upon the extent of the resection. Some surgeons have reported even higher recurrence rates following Billroth II resections for duodenal ulcer.

In recent years, it has been pointed out that the recurrence rate following the Billroth I operation for duodenal ulcer is considerably greater than after the Billroth II operation of the same extent. Ordahl and his associates [Ordahl, N. B., Ross, F. P. and Baker, D. V., Jr.: The Failure of Partial Gastrectomy With Gastroduodenostomy in the Treatment of Duodenal Ulcer. *Surgery*, **38**:158-168, 1955] report an incidence of recurrent ulcer of 18 per cent following the Billroth I operation for duodenal ulcer. Goligher and his associates [Goligher, J. C., Moir, P. J. and Rigley, J. H.: Billroth I and Polya Operations for Duodenal Ulcer–A Comparison, *Lancet*, **1**:220, (Feb.), 1956] give a somewhat similar figure and point out that their recurrence rate following the Billroth II operation in the same clinic was in the area of 2 per cent. Similarly Swedish surgeons are reporting a recurrence rate following the Billroth I resection in the area of 10 to 11 per cent when the procedure was performed for duodenal ulcer (Sten Wallensten, personal communication, October 1956). The reasons for this difference, granted a similar extent of excision of the acid secreting area of the stomach, are not apparent. The higher incidence of delayed emptying of the stomach following the Billroth I operation suggest that a narrow stoma may have something to do with the greater recurrence rate. One would naturally think that the reestablishment of the normal pattern of gastric evacuation through the duodenum should have many advantages. It is easier obviously to provide an adequate lumen after the Billroth II than after the Billroth I procedure.

In our country at the present time, the Billroth I and II operations are being more frequently combined with vagotomy. Some surgeons are advocating antral excision complemented by vagotomy. Whether such operations will protect against recurrent ulcer remains to be seen. It is apparent from current reports that, the addition of vagotomy pyramids the value of gastric resection in protecting against recurrent ulcer.

In our clinic, we continue to be partial to segmental resection for all ulcers save the antral ulcer. For the difficult duodenal ulcer, segmental resection has distinct technical advantages. Moreover, it is the only operation for duodenal ulcer following which we have observed no recurrences. Encouraged by a very satisfying experience with segmental resection as far as cure of duodenal ulcer is concerned, we have decreased the amount of acid-secreting area of the stomach sacrificed at operation. Whereas in the beginning (1949 to 1952), we excised in the area of 85 to 90 per cent of the acid secreting area, I now leave a fundic pouch representing approximately 30 to 40 per cent of the stomach. In addition, the antrum is left, which segment comprises in the area of 15 to 20 per cent of the intact stomach. That is to say, a residual gastric pouch remains constituting approximately 45 to 60 per cent of its original size.

In other words, we are leaving currently a residual fundic pouch larger than one would leave in an ordinary Billroth operation. It is obvious therefore that, I feel that the antrum, when left in continuity with the residual fundic pouch, adds protection. It is antral *exclusion* and not *retention* which potentiates ulcer recurrence following gastric resection.

At the same time, I probably should indicate that our experience with tubular gastric resection has not been as good as following segmental resection. The reasons are not apparent. Whenever one transects the stomach, one vagotomizes the segment distal to the site of transection. That, undoubtedly, is one of the reasons that German surgeons of half a century ago found segmental resection unacceptable; however, they felt that segmental resection was an inadequate operation and gave it up on that account. After the initial technical skirmishes with segmental resection, I found it necessary to add a routine Heineke-Mikulicz pylorotomy to insure ready emptying of the stomach.

In tubular resection, the entire lesser curvature is left intact. Without question, this is one of the items which contributes to the difference in behavior between segmental and tubular resection. Even the addition of division of the vagal twigs to the antrum, however, does not account solely for the difference. I have the feeling that the tent-like structure of the lesser curvature which frequently results following tubular resection, owing to the circumstance that the lesser curvature becomes the longer segment—that this circumstance makes tubular resection a periodic physiologic antral exclusion operation. If such should prove to be the case, obviously it would be unsafe to make such recess-

like closures of the stomach involving the antrum in any type of gastric resection.

I hesitate to digress to this extent in the discussion of the surgery of peptic ulcer; however, in any discussion of the subject, some comment upon the type of operation contemplated, I believe, is in order.

Dr. Charles A. Flood:—Thank you very much, Dr. Snapper and Dr. Wangensteen.

I agree fully with Dr. Snapper about the fact that one should try to make a diagnosis before instituting treatment, in any disorder. Unfortunately, we haven't reached this ideal in gastric lesions.

With regard to the question whether to operate on all or most patients with gastric ulcer, I think we can really boil the matter down to the risk. Such concepts as the risk of the surgery, the cure rate to be expected if the lesion is malignant vs. the outlook if the lesion turns out to be a benign one are considered. The mortality rate in surgery for gastric ulcer has dropped tremendously in the last 20 years, and the procedure now carries a very small risk indeed, in most patients. We always, however, are running into problems of people with coronary disease, emphysema, and so on, and we must be in position in individual cases to consider the risk of the operation as against the chances of a successful result if the lesion is a malignant one.

I think there the matter has to rest at the present time. One will always have to decide each individual case on its own merits and on the basis of the environment in which the patient is being treated.

Gastroscopy, Dr. Wangensteen, in our experience has been helpful in certain instances of patients with lesser curvature ulcer. For example, where the gastroscopic findings strongly suggest the possibility of malignancy, we have been enabled to avoid the test of healing, and save time for the patient. Gastroscopy is a procedure, however, which may not settle the diagnosis. This is also true of cytological studies of the gastric contents. These are procedures which are only accessories in diagnosis and may help if they really suggest a positive diagnosis of malignancy, but negative findings do not resolve the problem for us.

I have a question from the floor: would the size of a lesser curvature ulcer, as seen radiographically, give any indication as to its probable benignancy or malignancy?

There is data in the literature in favor of the view that larger ulcers of the stomach are more likely to be malignant. This, however, is, not universally true. The size alone of the ulcer is of very little help in deciding the individual problem, and if one wants to handle the problem conservatively, the fact that

an ulcer is, for example, more than 2.5 or 3 cm. in diameter should not prevent one from doing so.

Dr. Wangensteen:—I should like to ask Dr. Flood what operation he favors in a patient who needs operation for duodenal ulcer.

Dr. Flood:—For duodenal ulcer, Dr. Wangensteen, I favor some type of subtotal resection of the Billroth II variety. In speaking on this subject, I have no firsthand experience with it, and actually have to be guided by the judgment of my surgical colleagues.

The Billroth I procedure has been coming into vogue to some degree again, particularly on the basis of the fact that it is suggested that there is lessened tendency to some of the postgastrectomy symptoms after gastroduodenostomy hookup, as opposed to the Billroth II type of procedure. I think one must have reservations about whether this will turn out to be so, with larger experience. Vagotomy in our own institution has been used chiefly in association with a partial gastrectomy, and not with the other types of ulcer operation.

NEUROMA IN A DILATED STUMP OF THE CYSTIC DUCT, PREOPERATIVE VISUALIZATION BY INTRAVENOUS CHOLANGIOGRAPHY

JULIUS ROSENBERG, M.D., F.A.C.G.

and

MILTON J. MATZNER, M.D., F.A.C.P., F.A.C.G.

Brooklyn, N. Y.

The recent introduction of intravenously injected sodium iodipamide (Cholografin) has offered a rapid, reliable and safe medium for the roentgenological visualization of the entire biliary tract[1] and promises to be extremely helpful in the study of patients with digestive complaints persisting after cholecystectomy[2].

Among the conditions included in the possible etiology of the so-called postcholecystectomy syndrome or "recurrent biliary tract syndrome"[3] are: spasm of the papilla of Vater, recurring pancreatitis, common entrance of the pancreatic ducts into the papilla of Vater with pancreatic reflux, disturbed innervation of the extrahepatic biliary duct system, stones in the common bile duct, residual cystic duct stump[4], and neuromas in the region of the cystic duct stump and adjacent common duct[5-7]. The last condition has only been described during the past few years and is a diagnosis that is extremely difficult to make preoperatively. Although calculi in a dilated stump of the cystic duct have been visualized preoperatively by oral cholecystography and intravenous cholangiography[2,8,9], we can find no previous record of a neuroma in the dilated stump of the cystic duct visualized preoperatively.

The following case is reported because of the rather unusual preoperative demonstration of a neuroma within a dilated stump of the cystic duct 15 years after a cholecystectomy.

Report of a Case

D. J., a 53-year old married white male was first seen on 6 August 1953, by one of us (M.J.M.), complaining of recurrent bouts of severe pain in the epigastrium associated with vomiting, of four months' duration. His past history revealed a cholecystectomy 12 years previously. He had had an appendectomy in 1930 and an operation for right kidney ptosis in 1932. He had felt well for about four years after his cholecystectomy but about eight years prior to our first examination had noted the onset of his present symptoms which were intermittent with interval free periods of several weeks. For the four to five month

From the Division of Gastroenterology of the Department of Medicine, The Jewish Hospital of Brooklyn.

period prior to this examination he had almost continuous epigastric pain and he vomited soon after eating, with no evidence of food from previous meals in the vomitus. Nausea was marked but there was no weight loss. Physical examination at this time revealed a tense individual with negative physical findings. Urinalysis, blood count and serology were normal. Gastric analysis revealed a low degree of acidity. An intravenous pyelogram and an upper gastrointestinal x-ray series were negative. Oral cholecystography revealed no visualization of the gallbladder. The clinical impression at this time was no demonstrable organic disease with a marked functional element and with a possibility of coexistent chronic gastritis, chronic pancreatitis or common duct stones. He was placed on a bland diet, antacids, sedatives and antispasmodics.

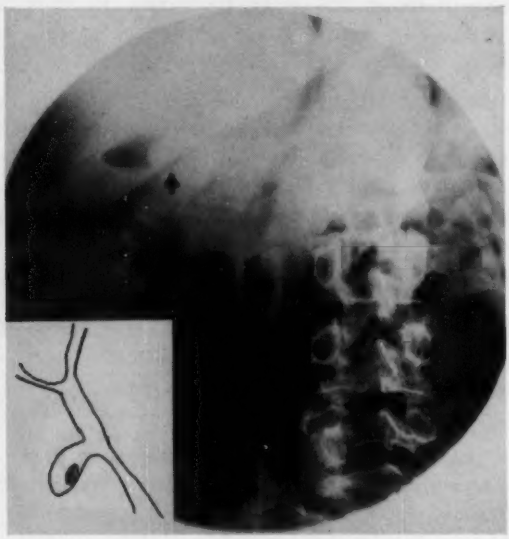

Fig. 1—Intravenous cholangiogram, with diagrammatic representation, of "re-formed gallbladder" with small negative shadow. Arrow indicates "re-formed gallbladder".

He was fairly comfortable until 6 May 1955 when his symptoms recurred. Intravenous cholangiography was performed and revealed a "re-formed" gallbladder within which there appeared to be a small negative shadow (Fig. 1). There was no dilatation of the common duct. A recheck upper gastrointestinal x-ray series was negative for organic disease.

Intermittent vomiting and epigastric distress continued under medical management and on 4 July 1955 he was admitted to the Jewish Hospital of Brooklyn for surgery. At that time he complained of pain in the epigastrium and the right upper quadrant of the abdomen of three months' duration. There was no radiation of pain, no fever, no jaundice and no abnormalities of the stool.

Physical examination on admission to the hospital revealed tenderness in the right upper quadrant of the abdomen. Laboratory tests revealed an icterus index of 6.0, a total bilirubin of 0.6 mg. per cent, a total cholesterol of 152 mg. per 100 c.c. with a free cholesterol of 39 mg. per 100 c.c. (25 per cent) and a prothrombin time of 11.0 seconds with a control of 10.7 seconds. The fasting blood sugar was 360 mg. per cent and the blood urea nitrogen was 22 mg. per cent. The urine revealed one plus and two plus albuminuria on two occasions.

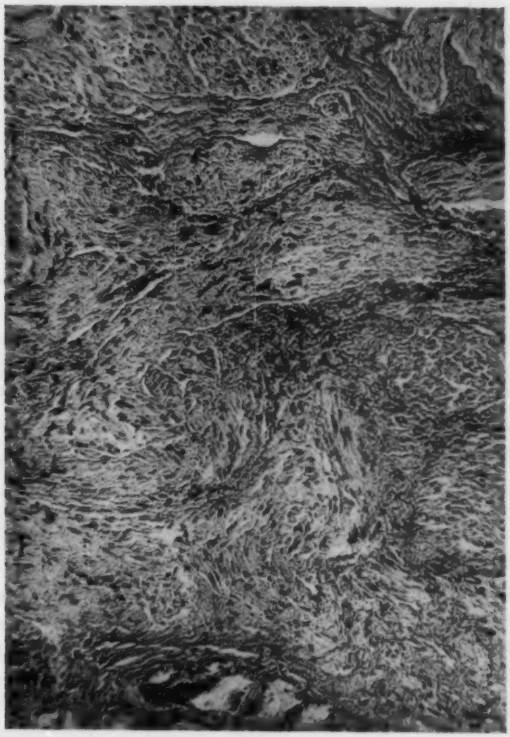

Fig. 2—Photomicrograph of neuroma of gallbladder found at operation; hematoxylin and eosin; x 150.

The blood Mazzini was negative. The hemoglobin was 14 gm. and the white blood count was 8,600 with a normal differential.

He was operated on 5 July 1955 and at operation the common bile duct was normal in size and not dilated. Palpation revealed it to be free of calculi. The cystic duct remnant was about 3 cm. in length and 0.5 cm. in diameter. There was a hard firm mass located within it. The cystic duct was removed *in toto*.

The gross specimen was described as a pink, red globular portion of moderately firm tissue measuring 0.9 cm. in diameter. The microscopic section (Fig. 2) was described by the pathologist, Dr. David Grayzel, as follows: "The preparation consists of fibrous and fibromuscular tissue which in places is infiltrated by inflammatory cell, mostly lymphocytes. In some areas are seen ducts which show no features of note. Many nerve bundles are seen. Diagnosis: tissue from cystic duct with chronic inflammatory reaction and with neuroma".

The patient had an uneventful postoperative course and was not seen again until 27 October 1955 when he reported for follow-up. He had felt well until three weeks before (about a two-month period of relative comfort) when epigastric discomfort and vomiting returned. A recheck upper gastrointestinal x-ray series was done on this date and was negative.

There was no relief of symptoms and on 3 November 1955 a gastroscopy was performed. Superficial and hypertrophic gastritis (subacute gastritis) was found.

On 10 November 1955 the patient came under the care of Dr. William C. Jacobson, to whom we are indebted for the following information. The patient continued to complain of severe pain in the epigastric region associated with vomiting, for which he had to take Demerol in order to sleep. He was admitted to the Jewish Memorial Hospital where he improved under treatment with sedatives, infusions and a very soft small diet. Two weeks after discharge, however, his symptoms recurred and on 23 January 1956 he was readmitted to the Jewish Memorial Hospital where he was operated on by Dr. Benjamin Sherwin who made the following observations: "the patient presented a tremendous blocking of the entire right upper quadrant by adhesions, causing angulation and a traction diverticulum of the first part of the duodenum, about ½ cm. in thickness. The entire duodenum, first and second portions, was drawn up into the denuded area of the gallbladder, causing kinking of the stomach and first part of the duodenum, which undoubtedly accounted for the severe vomiting." The stomach and duodenum were freed by careful dissection. The foramen of Winslow was examined and the common duct was identified; no calculi were found. The pyloric ring was identified and found to be patent. A vertical incision was made in the first portion of the duodenum to make certain to rule out a duodenal ulcer and stenosis.

The patient had a normal postoperative course, was able to eat and was discharged home. He was last seen by Dr. Jacobson on 28 February 1956. He had gained weight and was eating a regular soft diet. He still, however, complained of some pain in the right epigastric region if he overloaded his stomach.

Comment

From 5 to 20 per cent of patients with characteristic symptoms of cholelithiasis and/or cholecystitis and with the classical pathologic findings at opera-

tion will continue to have their symptoms in varying degrees of severity following cholecystectomy[7]. In 1946 Cieslak and Stout[10] mentioned the first recorded case of a neuroma of the dilated stump of a cystic stump following cholecystectomy and added another possible etiological factor for the postcholecystectomy syndrome.

In 1947 Womack and Crider[7] reported six more cases with similar pathological findings. Each of these patients had had a cholecystectomy followed by a recurrence of symptoms which were so severe that a second operation was advised. In four cases the cystic duct stump was identified. It was hard and fibrous and the site of an amputation neuroma. The neuroma was confirmed in each case by microscopic examination. In the remaining two patients neuromas in the periductal tissues were demonstrated.

It has been recognized[11-15] that a "re-formed gallbladder" may develop from dilatation of the cystic duct following cholecystectomy and that this may undergo pathological changes and be responsible for pathological complications and produce symptoms in the same manner as a diseased anatomical gallbladder.

In a recent review[16] of 35 cases of cystic duct remnant it was pointed out that a cystic duct remnant is the result of an inadequate cholecystectomy. Intravenous cholangiograms were performed on 121 patients following cholecystectomy and cystic duct remnants were demonstrated in 24 patients. It was pointed out that intravenous cholangiography is a valuable adjunct in demonstrating a cystic duct remnant, but that this condition is only one of several conditions that may be the basis for complaints after cholecystectomy. The symptoms may be undistinguishable from those of gallbladder disease. The persistence or the reappearance of symptoms following cholecystectomy should lead one to suspect a cystic duct remnant. In several cases the authors[16] observed a great number of large nerves around the cystic duct remnant.

Womack and Crider[7] stated that it was not the persistence of a large cystic duct *per se* that produced disability but rather the inclusion in the scarred walls of that duct of bundles of nerve fibers, chiefly sympathetic in type with perhaps a smaller number of vagal fibers. At times, fibrous tissue proliferation may result in a nodularity resembling the classical form of amputation neuroma. Also nerve trunks may become enmeshed in scar tissue in the region of the stump of the cystic duct. Such neuromas about the cystic duct may show evidence of acute or chronic inflammation. The scar tissue around the nerve trunk may stretch or strangulate the fibers and thereby produce symptoms[17].

Shafiroff and Hinton[18], in a discussion of the surgical anatomy of the choledochol nerves, present the nerve distribution of the gallbladder and surrounding structures and discuss surgical denervation of the *ductus choledochus* as a method of treatment for biliary dyssynergia. The nerve supply to the gallbladder and its ductal system is composed of sympathetic and parasympathetic nerve

fibers, the former through the celiac plexus and the latter through the vagus nerve. These nerves intermingle to form the anterior and posterior hepatic plexuses which are located about the region of the union of the cystic and common bile ducts. Nerve fibers from the anterior hepatic plexus usually follow the ramifications of the hepatic artery and its branches, while the posterior hepatic plexus fibers are found along the portal vein. The pain fibers supplying the biliary tract accompany the hepatic and cystic arteries to the gallbladder[8].

Womack and Crider[7] concluded from a review of the literature that stimulation of the sympathetic fibers will produce epigastric pain, while vagal stimulation will chiefly result in dyspepsia and vomiting. They also state that as a general rule several months usually elapse after the cholecystectomy before the recurrence of symptoms begins to appear. They felt that this would be in keeping with the laying down of the dense collagenous scar. They discuss their knowledge of many cases in which these postcholecystectomy symptoms have appeared and after a few years disappeared which they interpret as being due to complete degeneration of the damaged nerve trunks.

Amputation neuromas may occur at any site and were first described following traumatic amputations especially after wars. "Amputation neuromas always occur at the distal ends of the proximal segments of severed nerves and are characterized by a neural enmeshment in an overgrowth of the Schwannian sheath cells[6]."

Troppoli and Cella[17] discuss two cases in which amputation neuromas in the cystic duct remnant were the only etiological factors in the production of the postcholecystectomy syndrome. Both cases were confirmed by microscopic examination and both patients were asymptomatic one year after reoperation.

Stembridge[6], who presents a case of amputation neuroma following cholecystectomy, states "the possibility of an amputation neuroma should be kept in mind when patients with postcholecystectomy symptoms are seen clinically." Hume and Buxton[5] in reporting nine cases of postcholecystectomy amputation neuroma review their clinical features. In general, the recurring episodes of pain which mark the presence of a neuroma have appeared within a few months of the operative trauma which induced them. Both Troppoli and Cella's[17] cases had symptoms soon after cholecystectomy. The reappearance of symptoms as long as one or more years after operation is unusual. The outstanding feature in Hume and Buxton's[5] patients was severe right upper quadrant pain not easily distinguished from biliary colic, often requiring narcotics for relief and usually associated with nausea and vomiting. The usual preoperative diagnosis was a calculus in the common bile duct and the amputation neuroma was an unexpected finding. After operation and surgical removal of the cystic duct remnant and its associated amputation neuroma there was complete relief of symptoms. They conclude that injury of nerves immediately adjacent to the cystic duct may result in the formation of an amputation neuroma. The surrounding

inflammatory process may so alter the threshold of stimulation that symptoms are produced. "Little help is gained by the use of the standard roentgen and blood examinations[5]". They believe that this complication can be avoided by careful dissection of the sympathetic nerve fibers from the cystic duct before it is ligated. To minimize any pathological complications of the residual cystic duct stump that may "re-form" the cystic duct should be ligated close to the junction with the common bile duct.

On the other hand, Garlock and Hurwitt[4] are unconvinced that the amputation neuromas found in the scarred residue of the cystic duct are of any significance in the production of symptoms. In our case we cannot conclude that removal of the amputation neuroma in the cystic duct stump was ineffectual. It may have been beneficial as evidenced by the two-month period of comfort after its removal. The return of symptoms may have been due to adhesions that formed after this operation. The interest in the case herein reported is the visualization of the neuroma in the dilated stump of the cystic duct by intravenous cholangiography. Two extensive reports[2,19] of the use of this new diagnostic modality in the postcholecystectomy syndrome fail to mention any description of this unusual finding.

Summary

1. A case is presented in which there was preoperative visualization of an amputation neuroma in a dilated stump of the cystic duct by means of intravenous cholangiography.

2. The clinical significance of postamputation neuromas of the gallbladder still awaits further study.

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CHARACTERISTICS OF FAT-SPLITTING ENZYMES IN HEALTH AND DISEASE*

S. KATZ, M.D.†

Buenos Aires, Arg.

The present work was undertaken in order to clarify the characteristics of certain serum enzymes in normal conditions and in pancreatitis, to determine the significance of changes in their levels in relation to clinical diagnosis, and to establish simple and accurate methods for their determination. We have been interested particularly in the serum lipases and esterases, including the newly discovered heparin-induced clearing factor (C. F.).

Esterases are enzymes capable of hydrolyzing esters of carboxylic acids. Their classification by Richter and Croft[1] is generally accepted, dividing them into esterases proper (liver type of esterase, hydrolyzing preferentially short fatty acids); lipases (pancreatic type, hydrolyzing fat, olive oil and long chain fatty acids esters of alcohols, phenols and napthols); cholinesterases (including pseudocholinesterase, which hydrolyze choline and other esters), and true cholinesterase (with preferential action on acetylcholine). While the esterases proper and the lipases are relatively insensitive to eserine, low concentrations of this drug (10^{-5}M) inhibit the cholinesterases. The hydrolytic effects of the pancreatic type of lipase are increased manyfold by bile salts.

No enzyme acts exclusively on only one single substrate. Enzyme specificity means that an enzyme attacks a certain substrate much more than other ones. Therefore, multiple enzymes, such as are present in human and animal serum, have overlapping effects, i.e., they hydrolyze one substrate most, but act also on others, although to a lesser degree. If such an enzyme is present in large concentrations, such side or overlapping effects may be considerable. We have attempted to limit or to abolish these with the use of enzyme inhibitors or accelerators. An example of this is human pseudocholinesterase. This enzyme is present in the human serum in large amounts and, as shown later, is responsible not only for the hydrolysis of some short chain fatty acid esters, but also to a certain extent for the hydrolysis of some long chain fatty acid esters.

This fact must be taken into account in determinations of the pancreatic type of serum lipase, which is present in only small amounts in human serum.

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†From the Department of Gastrointestinal Research, Medical Research Institute of Michael Reese Hospital, Chicago, Illinois, and the Department of Medicine, University of Chicago. Hospital Churruca, Buenos Aires, Argentina. Formerly Fellow of the Gustavus and Louise Pfeiffer Research Foundation and the Interamerican Foundation for Postgraduate Medical Education.

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The use of esters of different acid chain length as substrates is not always adequate for the characterization of esterases, and this explains in our opinion some of the failures in the determination of the serum lipase as a test of pancreatic function. Thus, in the choice of practical and reliable methods for the determination of the esterolytic serum enzymes, the use of small amounts of serum, short periods of incubation, colorimetric readings*, and the choice of a suitable substrate are important. The substrate should be hydrolyzed mainly

TABLE I

EFFECTS OF DRUGS UPON THE HYDROLYSIS OF ALPHA-NAPHTHYL BUTYRATE AND LAURATE BY LIVER, PANCREAS AND SERUM OF MAN AND DOG

Drugs	Human and Dog Liver		Human and Dog Pancreas		Human and dog Serum	Human Serum	Dog Serum	Dog Serum plus Taurocholate
	alpha 4	alpha 12	alpha 4	alpha 12	alpha 4	alpha 12	alpha 12	alpha 12
Sodium Arsanilate	000	000	0	0	0000	0000	No hydrolysis	0
Potassium Flouride	0000	00	0	0	000	000	No hydrolysis	0
Lux	0000	0000	Z	++	000	000	No hydrolysis	+
Eserine Salicylate	0	0	0	0	0000	0000	No hydrolysis	0
Sodium Taurocholate	000	Z	0	++++	0	0	++++	
Eserine plus Taurocholate						00	++++	

0 to 0000 indicate degrees of inhibition (0 denotes up to 10%, 0000 denotes 90-100% inhibition)

+ to ++++ indicate degrees of activation (+ denotes slight activation, ++++ denotes more than 700% activation).

Z indicates no effect.

by the enzyme to be detected, and it should allow the use of inhibitors in order to exclude overlapping effects of other enzymes.

Determinations of the pancreatic type of serum lipase have been extensively used in the diagnosis of pancreatic diseases[2-7]. Lately, serum pseudocholi-

*It is felt, that titrimetric methods are less accurate than colorimetric or turbidity methods.

nesterase has been studied in relation to hepatic disease[8-13], and the heparin induced clearing factor has received much attention[14-19].

The most common substrates employed for the determination of the pancreatic type of serum lipase are olive oil[2] and tributyrin[6]. In spite of being a physiological substrate, olive oil has several disadvantages; it requires a long period of incubation, normal values differ with different authors, and it is a titrimetric method. The most important disadvantage appears to be, that olive oil is hydrolyzed also by other enzymes, i.e., the C. F. which hydrolyzes this substrate fairly well. What is said of olive oil, applies also to the use of tributyrin. Here, to the inaccuracy of the titrimetric method, a poor specificity is added, because it is known that serum pseudocholinesterase is mainly responsible for the hydrolysis[1].

The introduction of alpha and beta naphthyl compounds[20-24] for the determination of simple esterases, pseudocholinesterases, and lipases, with the advantages of colorimetric readings, high sensitivity and short periods of incubation, marked an improvement in the determination of these enzymes.

In the present study, the alpha rather than the beta compounds were chosen as substrates, because with their use, the esterolytic effect of the pseudocholinesterase can be inhibited more completely by eserine and therefore more specificity of enzyme action is obtained.

From the naphthyl compounds, naphthyl butyrate (alpha 4) was chosen for the determination of pseudocholinesterase, because this enzyme hydrolyzes it at a rapid rate, dilutions of serum from 1/500 to 1/2000 are sufficient to give good readings and, as mentioned before, nearly 100 per cent of the hydrolysis can be inhibited by eserine. For the determination of the pancreatic type of serum lipase, naphthyl laurate (alpha 12) was used[24]; the lipase effect was activated with sodium taurocholate, and at the same time pseudocholinesterase was inhibited with eserine or Nu 683*, and other liver esterases with Lux†.

Besides the pancreatic type of serum lipase and the pseudocholinesterase, another type of esterase appears in the serum following injection of heparin (clearing factor, C.F.). A review of the literature[14-19] is beyond the purpose of this communication, but certain features will be mentioned. The so-called C. F. seems to be different from the pancreatic type of serum lipase, because it is inhibited by taurocholate, and it is different from serum cholinesterase, because it is resistant to eserine; it hydrolyzes mainly long chain fatty acid esters, like those contained in chylomicrons, milk, egg lipoproteins, olive and coconut oil, and it hydrolyzes the naphtholic compounds very poorly. The methods for determination of C. F. are based on the degree of clarification of turbid emulsions, or the estimation of free fatty acids released. Results on C. F. will be presented,

*Hoffmann-La Roche.

†Trade Mark of a liquid detergent, Lever Brothers.

determined with the use of a new substrate proposed by us, Tween 60[26]. The test is based on the determination of turbidity produced by the combination of free fatty acids (released by the hydrolysis of Tween 60) with $CaCl_2$.

This report presents certain characteristics of the human and dog serum pseudocholinesterases, pancreatic type of serum lipases, and heparin-induced C. F., determined with the use of naphthyl butyrate, laurate and Tween 60 respectively. The effects of experimental acute pancreatitis and of pancreatectomy on the levels of these enzymes were also studied.

Materials and Methods

Extracts were prepared from human and dog's fresh pancreas and liver, carefully homogenized with saline, frozen overnight, and centrifuged; the supernatant was used for the determinations. In the following, these extracts will be called "liver" and "pancreas". Specimen of human and dog's blood were allowed to clot, were centrifuged, and the serum was used. Acute pancreatitis was produced in dogs by the injection of their own gallbladder bile under pressure into the main pancreatic duct, which was then ligated. Pancreatectomy was performed in dogs, and they were maintained with diet and insulin.

TABLE II

Effect of Drugs on the Hydrolysis of Tween 60 by Pancreas, Liver, and Postheparin Serum

Drugs	Pancreas	Liver	Postheparin Serum
Na Lauryl sulfate 10^{-3}M	0	85	17
Eserine salicylate 1.5×10^{-4}M	50	5	5
Lux 0.625%	+30	92	15
D.F.P. 2.5×10^{-6}M	85	92	8
E 600 1.5×10^{-7}M	95	98	27
Heparin 5×10^{-4}M	57	51	5
NaCl 1 M	+95	46	+13
KCl 0.5 M	+120	31	+5

Each figure denotes the percentage of inhibition or activation (+) against a control considered 100%.

Heparin was injected intravenously (one dose of 20 mg. of Abbott solution for man and 1 mg. per kg. for dog), and samples of blood were drawn at various intervals of time.

Naphthyl-butyrate, laurate and Tween 60 were employed as substrates for the enzyme determinations[24-26].

The following inhibitors or accelerators were assayed (final concentrations in substrate mixtures in parenthesis): eserine salicylate (10^{-5}M, 1.5 x 10^{-4}); sodium taurocholate (4 x 10^{-3}M, 10^{-1}M); potassium fluoride (1.6 x 10^{-3}M); sodium arsanilate (10^{-3}M, 5 x 10^{-3}M); Di-isoprophylfluorophosphate, D.F.P. (10^{-6}, 1.3 x 10^{-6}); diethyl p-nitrophenyl phosphate E 600 (1.5 x 10^{-7}M, 10^{-6}M); quinine hydrochloride (2 x 10^{-3}M); Lux, 0.2 and 0.4 ml. of a 5 and .625 per cent solution; heparin (5 x 10^{-4}M); sodium chloride (1 M); potassium chloride (0.5 M); magnesium chloride (0.5 M), and sodium lauryl sulphate (10^{-3}M).

Results

In Table I, the effects of sodium arsanilate, potassium fluoride, Lux, eserine and taurocholate upon the hydrolysis of alpha 4 and alpha 12 by extracts of human and dog's liver, pancreas and serum are presented.

Alpha-naphthyl butyrate is hydrolyzed at a high ratio by "liver", "pancreas" and serum, but the enzymes responsible for the hydrolysis behave completely different under the effect of the different drugs. "Liver" is strongly inhibited by arsanilate, fluoride, Lux, sodium taurocholate, and is slightly affected by eserine. "Pancreas" is practically not affected by any of these drugs, and serum is inhibited by all, but mainly by eserine (10^{-5}M; 82 per cent in the dog and 96 per cent in man). A clear-cut distinction between "liver" and "pancreas" esterases and serum cholinesterase can be established with the use of this substrate.

"Liver" hydrolyzes alpha-naphthyl laurate (alpha 12) 20 to 30 times slower than alpha 4. This hydrolysis is inhibited by arsanilate and Lux, less by fluoride, and is practically not affected by eserine and sodium taurocholate. "Pancreas" is not inhibited by these drugs, and is activated by Lux and especially by sodium taurocholate (10 to 30 times). While human and dog "liver" and "pancreas" behave very similarly, human and dog's serum showed differences that explain why results in the dog cannot be applied to man, unless special precautions are taken as described by Gomori[24]. Normal dog's serum hydrolyzes alpha 12 little or not at all, but addition of sodium taurocholate, increases the reaction by more than 700 per cent, and the hydrolysis behaves similar to the one produced by "pancreas". Both are activated by sodium taurocholate and are resistant to eserine, fluoride and arsanilate. The use of alpha 12 with Na taurocholate gives the true values of pancreatic lipase in dog's serum. No overlapping effect is produced by pseudocholinesterase. The human serum pseudocholinesterase is able to hydrolyze the substrate to a certain extent, and this effect is inhibited nearly 100 per cent by eserine (10^{-5}M). When sodium taurocholate is added, there is an inhibition of nearly 30 per cent, instead of the considerable increase observed in the dog. The addition of eserine as well as

sodium taurocholate produced only a partial inhibition, instead of the nearly 100 per cent obtained when eserine alone is employed. A very small amount of an enzyme with the feature of the pancreatic lipase (resistant to eserine, activated by Na taurocholate) can be detected in human serum.

It may be noted that human serum contains 4 times as much pseudocholinesterase than dog's serum (hydrolysis of alpha 4). The amount of pancreatic lipase in human serum is very small (about 200 times less than in dog's serum), or not detectable at all. In the dog, the low values of serum pseudocholinesterase and the high values of serum lipase explain why, for practical purposes, no eserine is necessary to inhibit the overlapping effect of pseudocholinesterase upon alpha 12.

Table III presents the effects of pancreatitis on dog's serum lipase. An increase was observed in all specimens, ranging from 100 to 900 per cent above the controls. No correlation, however, was found between these values and the severity of the disease.

TABLE III

HYDROLYSIS OF ALPHA-NAPHTHYL LAURATE IN MICROMOLES OF NAPHTHOL LIBERATED PER ML. OF SERUM IN 1 HOUR, BEFORE AND AFTER THE INJECTION OF BILE INTO PANCREATIC DUCT

Dog Number	1	2	3	4	5	6
Preoperative	5	15	47	22	12	12
Postoperative	54	26	104	54	32	24

All samples of serum were activated with sodium taurocholate (0.04 M).

In three pancreatectomized dogs, serum lipase values decreased first, but after a few days or weeks they returned to control values. The characteristics of this enzyme resemble those of the pancreatic type of lipase. Undoubtedly, an extrapancreatic source must be responsible for its production.

Human serum lipase determinations were done using alpha 12 with eserine, sodium taurocholate, and Lux, as proposed by Gomori[24]. In 145 different sera studied, normal values ranged up to 0.26 micromoles of naphthol per ml. of serum and three hours of incubation. In a few patients with the clinical diagnosis of acute pancreatitis or chronic relapsing pancreatitis, values as high as 10 times the normal values were found. Surprisingly, one patient with cholelithiasis showed a curious enzymatic pattern in his serum. A very strong hydrolysis of alpha 12 was found, which was inhibited only 50 per cent by eserine instead of the usual 100 per cent. Sodium taurocholate inhibited it strongly, allowing exclusion of the pancreatic type of serum lipase; fluoride, arsanilate and Lux also had marked inhibitory effects. The resistance to eserine and the

sensitivity to the other drugs seemed to indicate the presence of an hepatic type of esterase in this serum. On the basis of such observations, Gomori proposed the use of Lux, in order to avoid overlapping effects of any hepatic type of esterase present in serum.

The heparin-induced clearing factor was assayed using Tween 60 as substrate. For routine determinations, 0.1 ml. of serum with two hours' incubation was used. No hydrolysis by normal human or dog serum occurred, but following the injection of heparin, the substrate was hydrolyzed, increasing turbidity being noticeable after 30 minutes. Though a completely straight line was not obtained, a good proportionality was found as a function of time and concentration of enzyme.

Table II shows the effects of different drugs upon the hydrolysis of Tween 60 by human "liver", "pancreas" and postheparin serum. At the concentrations used, "pancreas" is inhibited by eserine, D.F.P., E 600, and heparin, and is activated by Lux, and sodium or potassium chloride. "Liver" is inhibited to a different degree by all of these drugs (except eserine). The C. F. appears to be, in general, more resistant to inhibiting drugs (except to magnesium chloride), than the pancreatic enzyme that hydrolyzes Tween 60.

Comment

In our experience, the use of alpha-naphthyl butyrate for the determination of serum pseudocholinesterase appears to be a very suitable method. The amount of serum necessary is small, 1 ml. of 1/500 to 1/2000 dilution in dog and man respectively; the technic is simple, and results are reproducible. Controls with eserine (10^{-5}M) or Nu 683 (10^{-5}M) should be performed, in order to confirm the presence of pseudocholinesterase by the complete inhibition by this drug. Although a clinical evaluation of the determination of pseudocholinesterase in liver disease is beyond the purpose of this paper, a few points must be emphasized. Pseudocholinesterase values in normal human serum show a fairly wide range, and the enzyme is very sensitive to the effect of various inhibitors. As mentioned by Augustinson[26], barbiturates, sulfonamides, p-aminobenzoic acid, morphine, papaverine, strychnine, sparteine, ergot alkaloids, and thiamine, inhibit the enzyme. Low values of pseudocholinesterase have been found in other than liver diseases[9,27,28], in hypoalbuminemias, chronic tuberculosis[29], multiple sclerosis[30], anemia[31], neoplasm, pregnancy[32], ulcerative colitis[33], and other conditions. On the other hand, no pseudocholinesterase was found histochemically in rat liver[20], and in dog's liver only in the walls of the sinusoids[34]. In our experience, the amounts of pseudocholinesterase in extracts of human and dog's liver were very small (less than 30 per cent of the total esterolytic activity), and we believe that some of this activity is due to blood present in the veins and sinusoids or the extracted organs. Thus, although low values of this enzyme have been found in parenchymatous diseases of the liver, the physiological basis of this test still remains obscure.

The use of alpha-naphthyl laurate as substrate, with addition of eserine, Nu 683, taurocholate, or Lux, as proposed by Gomori[24], seems to be a very reliable test for the determination of the human pancreatic type of serum lipase. In the dog, overlapping effects are minimal when sodium taurocholate is used. The wide range of lipase values in the normal dog's serum makes establishment of control values imperative, before any effects of experimental interference is studied.

In the human, high values of the pancreatic type of serum lipase were found in acute diseases of the pancreas, but in chronic affections of this organ, poor or negative results can be expected. In the latter, better results may be obtained, when pancreatic juice or urine is used. We have found 30 to 100 times lower than normal control values of pancreatic lipase in the duodenal juice from cases of fibrocystic disease of the pancreas.

With respect to the postheparin induced C. F., the use of Tween 60 as substrate seems to be an easy, inexpensive, and reproducible method for the quantitative determination of the enzyme. The fact that the substrate is hydrolyzed at a very low rate by extracts of human liver and pancreas, implicates few risks of superimposed effects of other enzymes. The main source of this enzyme in man and dog remains unknown, and the clinical use of this determination requires further investigation.

Summary

Alpha-naphthyl butyrate, laurate and Tween 60 have been used as substrates for the determination of pseudocholinesterase, pancreatic lipase, and the heparin-induced clearing factor in human and dog's serum. Different inhibitors have been used for the characterization of these enzymes and results in experimental pancreatitis and pancreatectomy and in pancreatitis in man are discussed.

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President's Message

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The grass-roots of the American College of Gastroenterology are dominated by our governors.

They are the direct contact between our membership and the parent body at the local level. They carefully review every applicant for affiliation with our organization. They act as a protection and support against irregulars in our midst. They develop an interest in gastroenterology by advancing teaching, research and learning among the young men in their communities. They promote the concepts of the American College of Gastroenterology by developing clubs, societies and chapters in their areas. They serve as a liaison with allied organizations and cooperate in any way they can.

The regional meeting should be a creation of their ingenuity. It is an expression of gastroenterology in the region involved. The better papers and essayists should be recommended for presentation at the Annual Convention. It is the reason for increasing membership participation in our annual convention each year.

A segment of our public relations program is geared directly to the governors. They should make their status known to the officers of their county and state medical associations. In this way, they could serve as counsellors for programs whether they be medical meetings, radio or television. This relationship should be carried on to allied professions and community organizations. In this manner, funds for research could be obtained if and when they became available.

Yes, our governors are the most important group in our organization. Any governor who does not agree has not made the most of his opportunity.

Arthur A. Kirchner

NEWS NOTES

Fellowship Keys

Keys for *Fellows* of the American College of Gastroenterology have been authorized by the Board of Trustees. An illustration of the key is at the left.

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In Memoriam

We record with profound sorrow the passing of Dr. Walter Loewenberg of New York, N. Y., Fellow and Dr. Georges Brohee of Brussels, Belgium, Honorary Fellow of the American College of Gastroenterology. We extend our deepest sympathies to the bereaved families.

ABSTRACTS FOR GASTROENTEROLOGISTS

GASTROINTESTINAL TRACT

TOTAL GASTRECTOMY: AN EVALUATION: E. S. Brinthall, Kate Daum, R. C. Hickey, R. T. Tidrick and A. P. Wickstrom. J. Internat. Coll. Surgeons, 25: (Apr.), 1956.

The author evaluated a series of 58 cases that underwent total gastric resection between 1947 and 1954. Of these 50 were cancer, 3 lymphoma, 1 bleeding varices, 3 benign gastric ulcer, and 5 anastomotic leaks.

The technical procedures included the following:

1. Simple jejunal loop anastomosis—14 cases, 5 died, the 9 remaining did not do well, food intake was poor and only one gained back his preoperative weight.

2. The Roscoe-Graham reconstruction—17 cases with 2 deaths, about ⅓ complained of bile regurgitation, limiting food intake and causing esophagitis. Only 4 gained back their preoperative weight. One is alive 3 years after surgery, another 7 years and another after 7 years.

3. Roux-en-Y reconstruction—24 patients with 2 deaths. The over all results appear more favorable than the other types, the chief advantage being protection against the regurgitation of bile and pancreatic juice. They are also able to take food earlier and in larger quantities.

4. Direct esophagoduodenal anastomosis —3 patients, 2 died, all lost weight, and did not protect against regurgitation of bile and pancreatic juice.

Nutrition revolved mainly around food intake. Appetite was poor, especially where regurgitation of bile took place. Faulty fat absorption occurred early, but approached normal several weeks after operation. Proteins were well utilized in absence of stomach. Glucose tolerance curves showed a hyperglycemic curve in 8 nondiabetic patients. Calcium and phosphorus balance held to normal on regular food. Oral iron intake had to be increased. Thiamine and niacin balance had to be supplemented.

Macrocytic hyperchromic anemia developed in 2 cases and were controlled by Vitamin B_{12} and folic acid. No true iron deficiency was noted, but all received supplemental iron therapy.

In conclusion, the author states that the operative death rate is 16 per cent and is sufficiently low to justify its use but sufficiently high to militate against its routine procedure in gastric cancer.

LOUIS K. MORGANSTEIN

A REVIEW OF TWO HUNDRED GASTRECTOMIES: Gerald B. Reams. J. Internat. Coll. Surgeons, 25:421 (Apr.), 1956.

The author reviews a series of 200 subtotal gastric resections done at the Jackson Memorial Hospital between 1951 and 1954. Of these there were 191 subtotal, 3 radical subtotal, 4 total, and 2 esophagogastrostomies, with 28 deaths, a mortality of 11.5 per cent.

In the emergency gastrectomies for massive hemorrhage, the mortality was 36.1 per cent. Gastrectomies for cancer mortality, 20 per cent. If these were excluded the mortality rate was 4.7 per cent.

Morbidity was 22.5 per cent, the most common complaint being pulmonary disorders, discharge from duodenal stump and hemorrhage.

Previous surgery for ulcer was 25 with mortality of 25 per cent.

Most frequent reason for operating was duodenal ulcer with hemorrhage in 50 cases with 25 per cent mortality.

A duodenal ulcer was found in 127 cases and removed in 48 with a mortality rate of 8.3 per cent and morbidity of 7 per cent.

In 36 cases operated for massive hemorrhage the interval between admission and operation was 62 hours and the average for those who died was 132 hours.

In 146 cases 2,500 c.c. of blood was required with a mortality of 5.3 per cent. For the 54 requiring more than 2,500 c.c. the mortality was 28 per cent.

The author concluded that the mortality rate was higher for the surgeon who performs it occasionally than for the surgeon who specializes in this procedure. Mortality and morbidity are lowered if the ulcer is removed. An empirical subtotal, even if no bleeding is found, gives more satisfactory results. The mortality rate in emergency massive hemorrhage is lowered with the promptness with which surgery is performed.

LOUIS K. MORGANSTEIN

ESOPHAGUS

THE TREATMENT OF CARCINOMA OF THE ESOPHAGUS: Edward F. Scanlon, Charles J. Staley, William T. Moss and John M. Dorsey. Quart. Bull. Northwestern Univ. M. School, 30:144 (Summer), 1956.

The poor results of surgical treatment of carcinoma of the esophagus are caused by an insufficient resection of this organ. In almost half of all cases tumor is left in the remaining esophagus, therefore, a subtotal esophagectomy is preferred especially in lesions of the middle and upper third. At the same time the patient receives a gastrostomy. Following this operation intensive irradiation of the tumor-bed is administered. Due to the extensive removal of the diseased esophagus mediastinitis, which frequently complicates radiotherapy, is avoided. At a second operation a reconstruction of the esophagus is done by transecting the transverse colon and mobilizing the right half of the colon, placing it into the neck, anastomosing the cecum or a segment of the terminal ileum to the cervical stump of the esophagus and the transverse colon to the stomach. In this way the acid-pepsin digestion is greatly eliminated.

H. B. EISENSTADT

STOMACH

MASSIVE HEMORRHAGE FROM PEPTIC ULCER: Warren W. Francis and Paul T. Welch. Rhode Island M. J., 39:260 (May), 1956.

This is another brief review of 101 cases of upper gastrointestinal bleeding, presented by two surgical residents. They have divided the group into three classes: massive bleeding, 18; moderate, 29; mild, 54. The paper is concerned mostly with the surgical versus medical treatment of the massive bleeders. Those managed medically had a high mortality (67 per cent), while those managed surgically had a mortality rate of 33 per cent. As in most of the articles published, the exact criteria is not given. On examination of the deaths, only two in the medically treated group were actually due to hemorrhage. Of the others, two were from terminal carcinoma, and

pneumonitis. Of six medical cases, four died, of nine cases of emergency surgery, three died. This actually brings the medical figure to 33 per cent as well. The paper is of interest in that it again highlights the importance of team work of the medical man and the surgeon.

JOHN N. DILL

SUBSTITUTE FOR STOMACH AFTER TOTAL GASTRECTOMY: USE OF RIGHT HALF OF COLON: Karl C. Jonas. J. Internat. Coll. Surgeons, 25:558 (May), 1956.

Total gastrectomy for advanced carcinoma of the stomach is the operation of choice, but replacement of a suitable repository for food has long been a stumbling block.

The substitute stomach must of necessity be placed between the esophagus and the duodenum and have capacity and function to: 1. prevent anemia, 2. store adequate food, 3. allow regurgitation of bile ferments, 4. prevent the "dumping" syndrome, 5. allay reflex esophagitis, 6. diminish steatorrhea, 7. allow protein metabolism for complete nitrogen balance.

The Hunnicutt operation lends itself to all these requirements; 20 centimeters of the ileum with the right half of the colon are employed.

In the procedure the entire stomach with a portion of the esophagus and duodenum, the spleen, the gastrohepatic and gastrocolic omentum are removed, the proximal portion of the ileum is secured to the distal part of the colon, the ileocolon segment is rotated medially and counter-clockwise and the proximal portion of the colon is anastomosed to the duodenal stump, the distal portion of the ileum is then joined to the esophagus.

While survival rate has not been increased by this radical procedure, patient comfort, which is most important, has been materially improved.

J. EDWARD BROWN

INTESTINES

THE CONDITION OF THE MUCOSA OF THE LARGE INTESTINE IN SOME DISEASES OF THE STOMACH: M. Siurala and M. Tawast. Ann. med. int. Fenniae 44:231 (Apr.), 1955.

In this paper the authors attempt to correlate the condition of the mucosa of the large intestine and some diseases of the stomach. They state that the large intestine and stomach represent, from a developmental point of view, the initial pattern of the primitive gastrointestinal tract.

The authors studied 10 cases with pernicious tapeworm anemia, 7 cases of pernicious anemia, 6 cases of iron deficiency anemia, 22 cases of peptic ulcer, and 45 cases without signs of deficiency.

The conclusion was reached that the process which caused severe atrophic changes in the gastric mucosa seems not to affect to a greater degree the mucosa of the lower part of the colon.

This was true also with peptic ulcer.

In iron deficiency anemia changes of the mucosa of the sigmoid colon were common.

In pernicious anemia, where stomach changes were marked, less changes were found in sigmoid mucosa.

In general the primitive intestine epithelium is either more resistant to toxic agents than the highly differentiated gastric mucosa or maybe less exposed to toxins producing changes in the gastric wall.

I. H. EINSEL

LYMPHOSARCOMA OF THE SMALL INTESTINE: P. Hillemand, E. Cherigie, R. Viguie, R. Bourdon, E. Gilbrin and Abatzis. Semaine des Hopitaux de Paris 24: (20 April), 1955.

Lymphosarcoma of the small intestine are more frequent than was previously thought. The authors have observed five cases in recent years. On the x-ray film they appear under the guise of cauliflower tumors with big vegetations, developing in the intestinal

lumen, driving back the healthy mucus membrane, and provoking a voluminous diverticula aspect.

Metastases are usual with generalized adenopathy. Up to the present moment all treatment be it surgical or roentgeno-therapeutic is palliative, mustard gas has given interesting results in one case.

TUBERCULOSIS OF THE SMALL INTESTINE AND OF THE ILEOCECAL REGION: E. Cherigie, P. Hillemand, C. Proux and R. Bourdon. Semaine des Hopitaux 24: (20 April), 1955.

Intestinal tuberculosis, often localized on the terminal small intestine, is more and more rare and complicates tuberculosis of the lung or the neighboring viscerae. Specific lesions are a hypertrophy of "Peyer's plaque" of lymphoid masses and of lymphatic glands. These injuries have a destructive evolution (ulceration of "follicles" and of the glands) and are sometimes accompanied by agglutination of the intestinal loops and the neighboring elements. The reactional process can be of hyperplastic type (tuberculoma of Dieulafoy) with formation of sclerosis that generates stenosis.

The functional changes that accompany these lesions consist especially of hypotonia followed by a very spasmodic phase of the last intestinal loop, as well as the fragmentation of the opaque index in the jejunum and the ileum.

The pseudo-tumoral hypertrophic form often leads to a very complex discussion with cancer, or Crohn's disease. Modern methods of treatment have allowed the study of these forms of the highest radiologic interest.

ULCERATIVE COLITIS AND SECTION OF THALAMOCORTICAL FIBRES: P. Hillemand, R. Viguie, J. Nallet and J. Lunel. Bull. et Mem. de la soc. med. des Hop. de Paris 29: (30, 31 Dec.), 1955.

After Cattan, who was the first to advocate bilateral intracerebral infiltrations of procaine to destroy the thalamocortical fibres, the authors used this method to treat two patients affected by ulcerative colitis.

If the lesions are not reversible this operation transforms the general state of the patient and allows a secondary colectomy in much better conditions.

CROHN'S DISEASE—REGIONAL ILEITIS IN ITS SUBACUTE AND CHRONIC FORMS: P. Hillemand, E. Cherigie, Viguie and Andre. Semaine des Hopitaux de Paris 75:8 (20 Dec.), 1955.

Crohn's disease is characterized in its initial stages by an important hypertrophy of the follicles of the glands and of Peyer's plates. The ileocecal region is the elective site of this malady, but sometimes multiple lesions are seen, and ileus and jejunum can be touched.

In its acute forms Crohn's disease simulates appendicitis. While in its chronic form, which is more frequent, it presents successive periods of aggravation and improvement which lead to surgical treatment. This last cannot, unhappily, avoid a nearly systematic recurrence.

INTESTINAL OBSTRUCTION: Paul C. Hodges and Roscoe E. Miller. Am. J. Roentgenol. 74:1015 (Dec.), 1955.

The roentgenogram is the best nonsurgical means of demonstrating the presence of small bowel distention, but usually non-roentgenologic procedures must be employed to differentiate the distention of obstruction from that of several other conditions, including adynamic ileus. "Closed-loop" obstruction is most easily diagnosed when the loop contains air, but even when it is filled solidly with fluid, the loop may show as a pseudotumor. Occlusion of mesenteric vessels, whether arterial or venous

and whether occurring independently or as a complication of obstruction, unfortunately gives little roentgen evidence of its presence. In obstruction of the colon, usually the ileocecal valve prevents reflux of gas and fluid into the small bowel but sometimes the valve is congenitally incompetent. Pneumoperitoneum is a frequent but by no means invariable concomitant of intestinal perforation and properly made chest films can be depended upon to demonstrate even very small amounts of free peritoneal air.

FRANZ J. LUST

LIVER AND BILIARY TRACT

AN ATOMOCLINICAL STUDY OF A CASE OF HANOT'S DISEASE WITH BIOPSY OF THE LIVER AND SPLEEN: C. Pera Blanco-Morales and A. Vinuela Herrero. Revue Internat. d'Hepatologie 5:1099, 1955.

The authors trace the historical evolution of the present day concept of Hanot's disease which, since its first description in 1875 has passed through three stages: a) V. Hanot's "hypertrophic cirrhosis with icterus", b) what was called "Hanot's cirrhosis" in the complex group of biliary cirrhoses, c) the present concept of "Hanot's disease" under the heading of reticulopathies.

Histological study of the liver: a) Healthy, noncirrhotic parenchyma; b) typical lymphonocytary nodosity; c) Clear dilatation of the vascular cavities full of lymphocytes; d) Fibroreticular hyperplasia; e) Diffuse hyperplasia of Kupffer's cells. In the spleen, hyperplasia of the cords of the pulp. The diagnosis of Hanot's disease was based on the following facts: a) smooth, soft hepatomegalia not accompanied by signs of portal hypertension and splenomegalia; b) periods of high fever alternating with afebrile periods and an increase in the rate of sedimentation; c) absence of a precise etiology; d) existence of histological lesions in the liver and spleen corresponding with fibroreticulosis; e) a slight disturbance in the functioning of the liver. The authors believe that the absence of icterus does not warrant dismissal of the diagnosis of Hanot's disease and brings into question the symptomatic category of this icterus.

FIRST CLINICAL AND BIOLOGICAL RESULTS OF THE TREATMENT OF ASCITIC CIRRHOSIS OF THE LIVER WITH PREDNISONE: R. Cattan and P. Vesin. Bull. et Mem. Soc. Med. Hopitaux de Paris p. 1146, 1955.

On the basis of previous investigations of the action of cortisone in liver insufficiency, which showed a strong action of this steroid on water disorders, the authors introduced Prednisone in the treatment of ascitic cirrhosis. The clinical and biological results seen in 9 patients can be classified as follows:

a) outstanding: the patient develops marked diuresis, sometimes of more than 3,000 ml. daily, loses his edemas and ascites. He remains free of edema after discontinuance of treatment. Such a result was achieved in three patients.

b) valuable: during treatment, the patient stops storing water, his bodyweight remains identical. Following discontinuance of treatment, edemas and ascites are increased again; this was noted in two patients.

c) bad: water accumulation goes on despite treatment. A better appetite and an improvement of the general condition, noted in all cases, are seen. This was the response of four patients.

Except for some contraindications (ulcer, nephritis), Prednisone represents a very valuable treatment of ascitic cirrhosis. In addition, it is an interesting means of investigation of the metabolism of water and electrolytes in ascitic cirrhosis.

BOOK REVIEWS FOR GASTROENTEROLOGISTS

PEPTIC ULCER—DIAGNOSIS AND TREATMENT: Clifford J. Barborka, M.D. and E. Clinton Texter, Jr., M.D. 290 pages, 33 illustrations. Little, Brown & Co., Boston, Mass., 1955. Price $7.00.

Dr. Barborka, who is Professor of Medicine and Chief of the Gastrointestinal Clinics, Northwestern University Medical School and Dr. Texter Jr., Associate in Medicine and Assistant Chief of the Gastrointestinal Clinics, Northwestern University School of Medicine, have written a book on peptic ulcer which embodies their own experience. The text is divided into 14 chapters with an appendix and extensive index.

They aptly state that physical examination is not of much help in diagnosis of ulcer. A careful history and x-ray examination and, in some cases, gastroscopy, will confirm the presence or absence of an ulcer. Gastroscopy is useful in questionable cases, especially in gastric ulcer or where there is doubt as to possible carcinoma. At times, it is difficult to differentiate from organs in close proximity to the stomach. We know peptic ulcer can simulate gallbladder or heart disease and/or pancreatitis.

There is a very interesting discussion by the authors as to the influence of hormones on gastric secretion, the role played by the antrum of the stomach in the increased output of hydrochloric acid thus causing gastroduodenal or gastrojejunal ulcers. The term peptic ulcer according to Barborka and Texter is in agreement with the reviewer's idea as to location of the lesions. Benign ulcers of the esophagus, stomach and duodenum when present, are regions bathed by the acid gastric juice, and the ulcer results from eroding action of the gastric juice. As to mechanical factors in production of these ulcers, it seems that they have a relation to the location of the ulcer, both in experimental animals and in human ulcer patients.

Whether or not heredity is concerned in ulcer production is a moot question. Incidence of ulcer in certain families is prone to occur more frequently. Emotional, economic and other factors in many families may be favorable to ulcer formation. The reviewer has patients in whose families ulcers are of frequent occurrence. More recently, ACTH and cortisone preparations precipitated ulcer symptoms or even hemorrhage. Neurogenic and personality factors are also conducive to ulcer formation.

Symptomatology and diagnosis are adequately described by the authors. The medical management including diet, alkalis and the cholinergic blocking agents with indications are concise. Recurrence of the ulcer, hemorrhage, complications and their management including surgical treatment, add to the value of this treatise.

The appendix deals with recipes and menus commonly used in ulcer management. The x-ray illustrations, the printing and the clear type make reading a pleasure.

THE CLINICAL RADIOLOGY OF THE ESOPHAGUS: Marcel Brombart, Chef du Service de Radiodiagnostic a la Clinique de Paepe, Brussels, Belgium. Introductions by Ch. Auguste and L. Deloyers. 466 pages, 337 illustrations, extensive index. Masson and Co., Paris, France, 1956.

The roentgenological examination is the most important and easiest one to demonstrate pathology of the esophagus. Brombart has had tremendous experience in this field and has published a great number of papers. He has written a book which will become one of the fundamental reference works. He describes the pharynx, the different parts of the esophagus and the cardia. There is a special chapter on functional troubles and on all pathological changes. Some other interesting points are extrinsic influences on the pharynx and the diverticula near the cardia. We would like to point out the chapter on esophagitis and the chapter on ulcers of the esophagus. There are 337 illustrations and all of them are clear and instructive, probably more instructive than those found in most other books. Each chapter has an extensive bibliography. The book is written in French. The print is clear and the illustrations are so good that even to someone who does not read French, the book is highly recommended. This book is also recommended to internists, gastroenterologists, radiologists and surgeons. The quality of the book is excellent.

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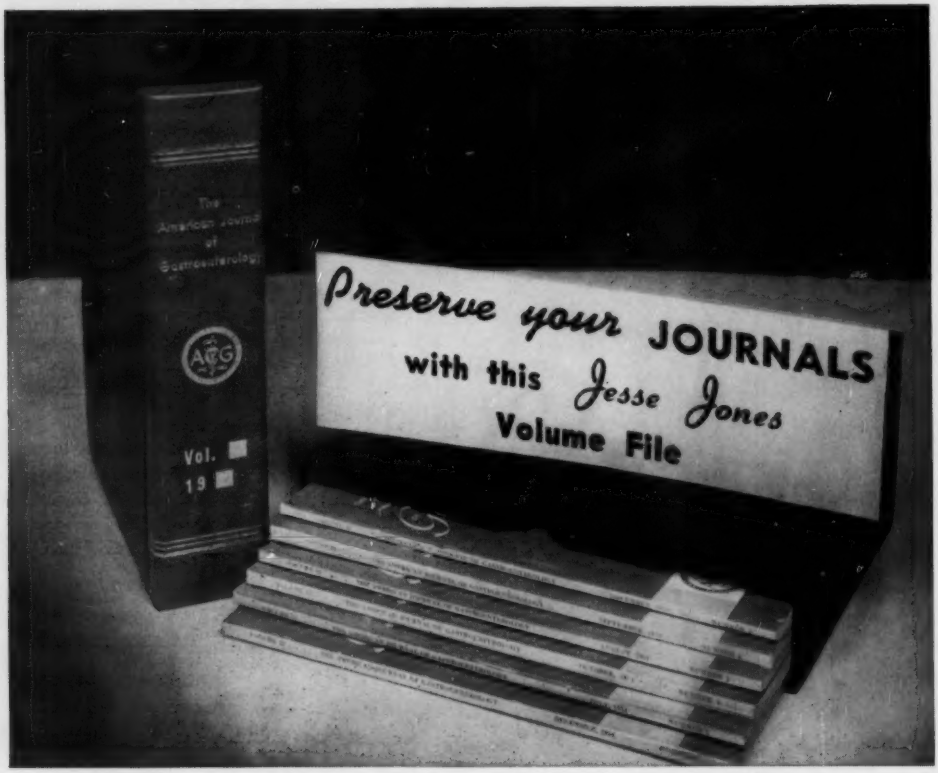

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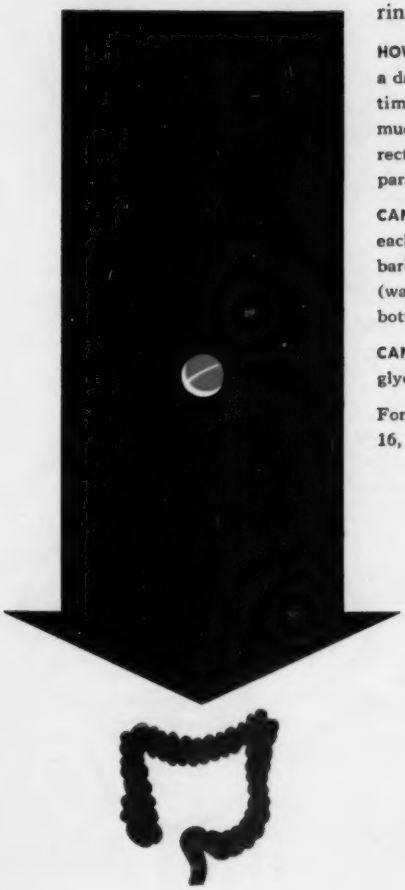

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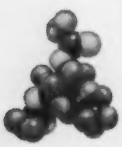

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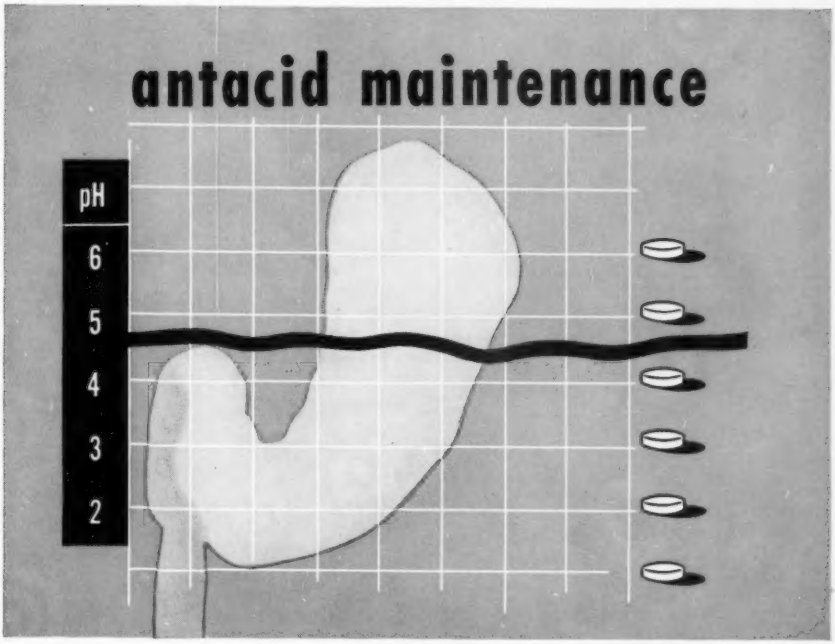

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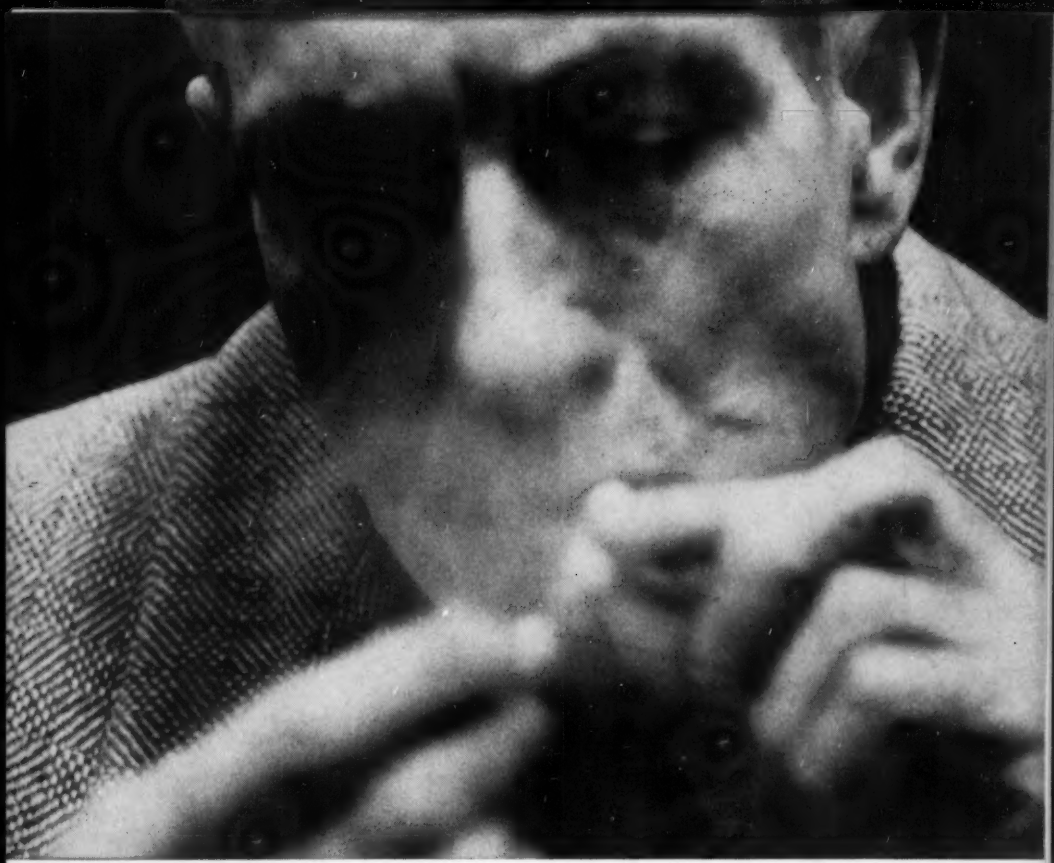

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